



D4.2. Training Manual on Research Ethics for Research Ethics Committee Members in Africa

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Using This Manual

Purpose of the Manual

This manual has been developed as a comprehensive training resource to support the ethical review of health-related research involving human participants. It is intended to enhance the capacity of Research Ethics Committee (REC) members, trainers, and stakeholders by providing conceptual clarity, practical guidance, and internationally grounded ethical frameworks. The manual is designed to respond to the increasing complexity and volume of research conducted globally—particularly in low- and middle-income settings—by equipping users with tools to carry out ethical review with competence, consistency, and ethical depth.

Audience

This manual is written for two key groups:

- **Trainees:** Individuals serving on or preparing to join Research Ethics Committees, including health professionals, researchers, ethicists, legal experts, lay members, and community representatives.
- **Trainers:** Those responsible for building ethics capacity through workshops, academic instruction, or institutional training, including faculty members, senior REC members, and ethics educators.

Both audiences are encouraged to engage the material as a dynamic resource that supports lifelong ethical learning and responsible research oversight.

Structure of the Manual

The manual is structured into six progressive modules. While each module can be used independently, they are designed to build cumulatively toward a comprehensive understanding of research ethics:

Module 1: Foundations of Research Ethics

Introduces the concept of research, distinguishes it from medical practice, and examines the importance of ethical oversight. It includes a historical overview of unethical research practices that led to the development of international research ethics guidelines.

Module 2: Ethical Principles and Theories of Ethics Applied in Research

Explores mid-level ethical principles (autonomy, beneficence, non-maleficence, and justice)

and broader ethical theories (deontology, utilitarianism, virtue ethics, and care ethics). These are presented as essential tools for ethical reflection and justification.

Module 3: The Role and Functioning of Research Ethics Committees

Describes the legal, procedural, and ethical responsibilities of RECs. It outlines their structure, operational independence, review procedures, and ethical obligations to both participants and researchers.

Module 4: Risk-Benefit Assessment and Risk Minimization in Research

Focuses on assessing potential risks and benefits to participants and third parties. It discusses principles of proportionality, strategies for risk minimization, and the importance of scientific and ethical justification.

Module 5: Vulnerability, Inclusion, and Justice in Participant Selection

Examines issues of vulnerability, fairness, and equity in participant selection. It explores safeguards against exploitation, the inclusion of marginalized groups, and the ethical significance of justice in health research.

Module 6: Informed Consent and Ongoing Ethical Engagement

Details the ethical and practical requirements for obtaining and maintaining valid informed consent. It includes considerations of capacity, comprehension, voluntariness, cultural sensitivity, and the ethical imperative for ongoing participant engagement.

Each module includes:

- A defined scope
- Learning objectives tailored to REC functions
- Explanations of core ethical concepts and frameworks
- Practical examples and applications
- A conclusion reinforcing key insights

Guidance for Trainers

Trainers are encouraged to use this manual as both a teaching resource and a facilitation tool. Effective training should:

- **Be participatory:** Incorporate group discussions, case studies, role plays, and ethical deliberation exercises.
- **Be contextualized:** Supplement with national guidelines, institutional policies, and culturally relevant examples.

- **Promote ethical reasoning:** Encourage trainees to think beyond checklists and procedural compliance, and instead focus on principled justification and value-driven decision-making.
- **Model interdisciplinary engagement:** Invite facilitators with varied professional backgrounds to reflect the diversity of REC composition and the range of issues under review.

The manual can be used in full-day training workshops, modular short courses, or integrated into ongoing REC education programs.

Recommendations for Trainees

Trainees should approach this manual not just as an instructional document but as a framework for reflective practice. You are encouraged to:

- **Engage actively** with concepts and discussions
- **Think critically** about the ethical tensions that arise in research review
- **Apply principles and theories** to real-life protocols
- **Consult referenced guidelines** (e.g., Declaration of Helsinki, CIOMS, Belmont Report) to deepen your understanding
- **Foster peer dialogue:** Ethical review is inherently deliberative; shared reasoning and respectful disagreement are vital to good REC practice

Final Note

This manual is a foundational tool for building ethical research oversight systems. It aims to promote a culture of ethical awareness, principled decision-making, and ongoing learning. Trainers and trainees alike are encouraged to treat the manual as a living resource, to be adapted, critiqued, and expanded in response to emerging ethical challenges and diverse research contexts.

Let this manual support your commitment to upholding the dignity, rights, and well-being of all those who participate in research.

1 Module 1: Foundations of Research Ethics

SCOPE OF THE MODULE

This module introduces the foundational concepts and rationale underlying research ethics, especially in health-related research. It begins by defining research and distinguishing it from other practices such as clinical care. It then explores different modes of knowledge production, highlighting how methodological diversity influences ethical oversight. The module emphasizes the essential role of ethical reflection in research involving human participants, introducing key ethical frameworks and the concept of Reflective Equilibrium. Through historical case studies—including the Nazi experiments, Imperial Japan's Unit 731, and the Tuskegee Syphilis Study—it illustrates how unethical research practices have shaped the evolution of modern ethical standards such as the Nuremberg Code, the Declaration of Helsinki, and the Belmont Report. This historical and conceptual foundation prepares REC members to engage more deeply with ethical deliberation in the modules that follow.

LEARNING OBJECTIVES

By the end of this module, REC members should be able to:

- Define research and distinguish it from related practices such as clinical care.
- Identify and compare different modes of knowledge production and their implications for research ethics.
- Articulate the value and necessity of research in advancing human health and societal well-being.
- Recognize the epistemological-ethical tension inherent in research involving human participants.
- Describe key historical events and ethical violations that led to the development of modern research ethics guidelines.

1.1 What is Research?

UNESCO, following the Frascati Manual¹, defines *Research and Experimental Development* as “creative and systematic work undertaken in order to increase the stock of knowledge – including knowledge of humankind, culture and society – and to devise new applications of available knowledge.”² UNESCO further specifies that R&D activities must satisfy five criteria, specifically the following: novelty, creativity, uncertainty, systematicity, and transferability and/or reproducibility.² Of the five criteria, the last one, i.e., transferability and/or reproducibility -- described by UNESCO as the quality of an activity “to lead to results that could be possibly reproduced”² -- may be controversial/contentious especially in qualitative research or research within the humanities largely because these knowledge production modes are less about numerical replication (think for example of immersion studies in anthropology or ethical

reflection in philosophy/ethics) but rather are more focused on other epistemic values such as on transparency, interpretative coherence, contextual richness, trustworthiness, among others. In such contexts, reproducibility is better understood not as the replication of identical results, but as the ability of other researchers to trace, understand, and critically engage with the research process and findings.

1.1.1 Distinguishing Research from Other Activities, Such as Medical Practice

It is quite easy to confuse research with activities such as medical practice because both activities may involve similar procedures, settings, and personnel. For example, clinical trials are usually done in hospitals involving medical procedures that are usually associated with clinical care, attended to by medical personnel. However, these two activities – medical practice and research, and in this example, clinical trials, are distinguishable in terms of purpose and expectations. Medical practice is meant to benefit the health and well-being individual patients while research is meant to generate generalizable knowledge, or, in the words of UNESCO, “to increase the stock of knowledge.” In terms of expectations, medical practice is expected to use proven treatments based on best practices to cure sicknesses in patients, and in this sense is patient-centric. Research, on the other hand, is expected to utilize scientific method (i.e., a systematic process of observing phenomena, formulating hypotheses, testing them through controlled investigation, and analyzing the results to draw evidence-based conclusions³) to arrive at generalizable knowledge, and, as such, is population- and/or hypothesis-centric.

1.1.2 Modes of Knowledge Production

Research is carried out in every discipline and through all modes of knowledge production. Within the sociology of science literature, the term *knowledge production mode* refers to the “the way (scientific) knowledge is produced,” i.e., distinct ways in which scientific and scholarly knowledge is generated, organized, and validated. Methods vary: researchers employ quantitative, qualitative, mixed methods, or employ methods used in the humanities such as conceptual, interpretative, critical/theoretical, or normative research. In Table 1, we demonstrate three knowledge production modes as reflected in the literature.^{4,5}

Feature	Mode 1	Mode 2	Mode 3
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Focus	Basic research, theory	Application, problem-solving	Integration of multiple knowledge modes
Disciplinarity	Disciplinary	Transdisciplinary	Inter- and transdisciplinary
Organization	Hierarchical, stable	Heterarchical, transient	Multi-level, networked
Quality Control	Disciplinary peer review	Broader, collaborative criteria	Multi-criteria, systemic
Context	Context-free	Context-driven	Multi-contextual
Researcher Role	Detached observer	Engaged, reflexive actor	Entrepreneurial, networked

Table 1: The Three Modes of Knowledge Production

To further exemplify the three modes, Table 2 provides examples of research within these three modes. All of the examples are relevant to human health.

Mode	Example	Description	Human Data/Participants	Context
Mode 1	Hospital-based clinical trial evaluating a new antihypertensive drug	Medical researchers recruit patients with high blood pressure, randomize them to receive the new medication or standard treatment, and measure outcomes such as blood pressure reduction and side effects.	Direct involvement of patients; data collected include clinical measurements, medical histories, and follow-ups.	Conducted within a single discipline (medicine), following established protocols and ethical standards.
Mode 2	Participatory research to improve maternal health in rural communities	Researchers, healthcare providers, local leaders, and women from the community collaborate to identify barriers to prenatal care, co-design interventions (e.g., mobile clinics), and evaluate impact through surveys and interviews.	Community members and patients are active participants and co-researchers; qualitative and quantitative data.	Integrates public health, social science, and local knowledge; focused on practical solutions and social accountability.
Mode 3	Multi-partner chronic disease	The project collects and analyzes diverse human data (e.g., electronic health	Thousands of individuals contribute health, behavioral,	Collaborative and dynamic; bridges clinical medicine,

	management initiative	records, wearable device data, community feedback) to co-develop and refine digital health tools and care pathways responsive to patient and system needs.	and experiential data; broad stakeholder involvement.	public health, data science, policy, and industry; systems thinking.
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Table 2: Examples of health-related modes of knowledge production

Research ethics committees (RECs) are created to safeguard the rights, safety, and well-being of research participants in research, in any and all knowledge production modes that include human data and/or human participants. Because this Manual is made primarily for members of RECs evaluating health-related research, the examples in Table 2 are purposely health-related.

1.1.3 The Necessity of Research for Advancing Healthcare

In Table 2, we provided examples of research activities, all of which are meant to learn more about human health for the purpose of improving healthcare. Indeed, research is a cornerstone of medical advancement. Through rigorous investigation, it provides the evidence base that underpins clinical guidelines, public health interventions, and health technologies. From developing vaccines to evaluating new surgical techniques or exploring genetic influences on disease, research drives progress and innovation in healthcare. Without research, medical practice would become stagnant, making it incapable of effectively addressing emerging health challenges or adapting to evolving patient needs. Article 5 of the [2024 Declaration of Helsinki](#) conveys this message by saying, “Medical progress is based on research that ultimately must include participants.”⁶ Guideline 1 of the [CIOMS International Ethical Guidelines for Health-Related Research Involving Humans](#), on the other hand, essentially conveys the same message that medical progress is based on research but also provides a concept that is often utilized in research ethics, i.e., that the scientific and social value of research is a necessary (but not sufficient) justification for research:

The ethical justification for undertaking health-related research involving humans is its scientific and social value: the prospect of generating the knowledge and the means necessary to protect and promote people’s health. Patients, health professionals, researchers, policy-makers, public health officials, pharmaceutical companies and others rely on the results of research for activities and decisions that impact individual and public health, welfare, and the use of limited resources. Therefore, researchers, sponsors, RECs, and health authorities, must ensure that proposed studies are scientifically sound, build on

an adequate prior knowledge base, and are likely to generate valuable information.⁷

1.2 Why is Ethical Research Important?

The value of research for medical care is undeniable, as we have emphasized above. However, this process requires human participation, may it be in the form of human data or the inclusion of human participants. This creates a tension between the epistemological goals of research (i.e., gaining knowledge) and the rights of human beings to dignity, equality, life, liberty, security of person, privacy, self-governance, among other rights enshrined at the [Universal Declaration of Human Rights](#). To say it succinctly, healthcare related research that entails human participation is always a struggle between epistemology and ethics. This creates the rationale for guidelines such as the Declaration of Helsinki, the CIOMS International Ethical Guidelines, the UNESCO [Universal Declaration on Bioethics and Human Rights](#), the [Belmont Report](#), [the Council of Europe's Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Biomedical Research](#), among other international and national guidelines. In this sense, ethics is important and necessary because research requires the participation of humans who, in turn, have inherent rights that must always be respected and protected.

Aside from the considerations of human protection which creates the epistemological-ethical tension we discussed above, there are also ethical and integrity requirements stemming from the nature of research itself. This is the area we call research integrity. This means that good and trustworthy research practice requires that researchers do not copy from others (plagiarism), do not invent their data (fabrication), do not manipulate their data (falsification), and many others elaborated on by guidelines such as the [European Code of Conduct for Research Integrity](#). For the intention of this Manual, we shall focus on considerations of human protection in research.

1.2.1 What is Research Ethics

Research Ethics systematically and transparently reflects on and provides reasoned justification for the acceptability or non-acceptability of research practices. Ethical justification, on the other hand, refers to the demonstration of rightness or wrongness, acceptability or non-acceptability of a case, position, or practice based on considerations of relevance and sufficiency of reason⁸ while considering *ethical principles/theories, moral intuitions, and relevant facts*.^{9,10} These three aspects of ethical justification came from a well-known method of ethical justification called Reflective Equilibrium that was originally proposed by John Rawls and revised by commenters such as van Delden and van Thiel.^{10,11} In the latter system, the three

aspects are to be mutually adjusted or balanced until a state of coherence or balance is reached.

1.2.2 What this means for REC members

For REC members, keeping in mind Reflective Equilibrium is informative in understanding what it means to do an ethical deliberation. Having all the necessary facts is just one of the requirements. It is also important to know where one is coming from (one's moral intuitions), the relevant ethical principles/theories, and explicitly deliberating on these aspects until a state of coherence/balance is reached on which the judgment is based. In Module 2, we shall elaborate on ethical principles and theories and how these principles and theories may be useful in the process of ethical justification.

1.3 History of Research Ethics

In the foregoing, we have demonstrated how ethics is, in fact, integral to research. This connection underscores the necessity for rigorous ethical frameworks that address the complexities of human participation in research, ensuring that the pursuit of knowledge does not compromise fundamental human rights and dignity. In what follows, we shall delve into the history of contemporary research ethics, exploring the pivotal moments and profound lessons that have shaped its evolution.

Research ethics was born from scandals. This means that this area of inquiry was born as a reaction to medical research malpractices that unfortunately led to the suffering and demise of countless human beings. From these tragedies, medical research ethics guidelines were drafted, ratified, and circulated. In this short account of the history of medical research ethics, we will look at three scandals that brought forth some of the research ethics guidelines that we are now most familiar with. We will look at the Nazi experiments and the experiments of the Imperial Japan both within the context of the Second World War, and the Tuskegee experiment. After discussing these three events, we shall then briefly discuss the guidelines that sprang from them.

Note that there are many other events that may be worth studying such as the Yellow Fever experiment, the Willowbrook experiment, the Salk Polio Vaccine experiment, among others. But, at least in this module, we limit ourselves to these three events for the purpose of demonstrating how some of our modern-day guidelines sprang from scandals.

1.3.1 The Nazi Experiments

The National Socialist German Workers' Party (Nazi) party came into power in 1933 when Adolf Hitler, the party's leader, was appointed Chancellor of Germany. From this appointment, Hitler quickly established a totalitarian regime known as the Third Reich¹².

The Third Reich is founded on the false belief that there was a pure Aryan Race (in this sense, referring to Caucasians), that modern-day Germans belong to this race, and anyone who is not part of the Aryan race is inferior. These false and highly racial ideological presuppositions led the Nazi party to be engrossed in demonstrating either the superiority of Caucasians or the inferiority of those who are not, but also in cleansing and purging Germany of the weaker races. This meant racial prejudice but also prejudice against individuals with mental and physical disabilities as well as the homosexuals, including the Caucasian Germans. It was within this background that we should understand the important role of Nazi Eugenics and the experiments associated with it. It should also be understood that these experiments were mostly associated with the Second World War. As such, the majority of the experiments were racial and/or war-injury related. We shall cite a few of these experiments with the caveat that some of the experiments are continuously discovered, and as such, the total number of victims of Nazi experiments remain unknown, with estimates ranging for 15,754 victims¹³ to much more¹⁴.

1.3.1.1 Examples of Medico-Military Experiments

In several of the concentration camps such as Auschwitz, Dachau, Sachsenhausen, Ravensbrück among others, brutally inhuman medical experiments were held. In Sachsenhausen, for example, prisoners were deliberately infected with epidemic jaundice, lost mustard gas, among others, for the purpose of understanding these diseases and to experiment on therapies. Many prisoners died and suffered in the process. Below are some of the most infamous of these experiments. For photographs of these experiments, please visit the [Holocaust Encyclopedia](#).

Freezing experiments: These experiments were held in Dachau and led by Luftwaffe (air force) chief surgeon Erich Hippke and Dr. Sigmund Rascher, with the approval and oversight of the Reich Leader (i.e., 2nd in command to Adolf Hitler), Heinrich Himmler^{15,16}. The rationale of the experiment was to find the most efficient way to address the hypothermia and other cold injuries that German soldiers suffer from in the Eastern front as well as the hypothermia suffered by German pilots who fall into the North Sea.

The experiment enlisted 300 prisoners, resulting to the death of 80 to 90 of them. To replicate the conditions of the Eastern Front and the North Sea, the prisoners were

forced either to remain outdoors in freezing weather for 14 hours or to be kept for up to three hours in icy water tanks. In the process, the Nazi scientists kept track of their pulse and temperature through electrodes. Several warming methods were tried, the most effective being that of immersion in hot water. In some instances, freezing prisoners were thrown into boiling water. As mentioned above, 80 to 90 prisoners died in the process. In one instance, Himmler told Rascher that normal fisherfolks from the North Sea region warm themselves in the company of their wives¹⁶. Because of this, four gypsy women from the Ravensbrück concentration camp were brought into the experiment, forcing them to be naked and placing some of the frozen prisons in between them¹⁶.

High altitude experiments: This experiment was meant to address high altitude sickness that pilots who bail out in high altitude experience and suffer from. The cause would be low oxygen in high altitude, with different degrees of severity in relation to lower availability of oxygen in higher altitudes. Altitude sickness can lead to pulmonary edema and/or cerebral edema.

Just like the freezing experiments, the high altitude experiments were also held in Dachau also by Dr. Sigmund Rascher^{15,16}. To simulate high altitude conditions from 10km to 20km above the ground, a decompression chamber was used and decompression adjusted to simulate the conditions in varying altitudes. In total, 200 prisoners were used in this experiment. The prisoners were placed inside these decompression chambers. 80 prisoners died outright while others were executed. In several instances, Rascher would dissect the brains of the then still alive prisoners, in an attempt to demonstrate the formation of tiny bubbles in the blood vessels of the subarachnoid part of the brain^{15,16}.

Sea water experiments: Because German pilots who bail out of their aircrafts and fall into the North Sea ingest sea water, the intent of this experiment was to understand the potability as well as the effects of prolonged ingestion of sea water. 90 Roma prisoners from Dachau were used in this experiment this time headed by Dr. Hans Eppinger and Dr. Wilhelm Beiglboeck. The Roma prisoners were given no other liquid but sea water. The prisoners of course suffered from severe dehydration, with some seen licking freshly mopped floors for non-salinized water¹⁵.

In another group, 44 prisoners were divided into four arms: no water, sea water, sea water processed by the Berka method (i.e., not desalinizing the water, but adding various sugars to render the taste more agreeable), and sea water without salt¹⁷. Aside from observation, the Nazi scientists also gathered data through liver or spinal cord

punctures¹⁷. Most if not all of the prisoners who were given sea water suffered severe dehydration, “diarrhea, convulsions, hallucinations, foaming at the mouth, and in most cases, madness or death”¹⁷.

Sulfanilamide experiments and experiments on the regeneration of bones, nerves and muscles: the German soldiers suffered from gas gangrene within the Russian front. Aside from gas gangrene, other infections were also prevalent during the war such as streptococcus and tetanus. Aside from infections, broken bones, tissues, and muscles are to be expected during war. To address these issues, the Nazis through Doctors Karl Gebhardt and Horst Fischer did two experiments on 15 prisoners who were transferred from Sachsenhausen to Ravensbruck and to 74 Polish women (who were called “the rabbits” since they were experimental subjects). The women were first experimented on in a medical institution near Ravensbruck, but after some time, the women understandably violently resisted being part of the experiments. As a consequence, they were brought to Ravensbruck where the last set of experiments were accomplished¹⁸. But, how exactly were the prisoners and the women experimented on?

The first set of experiments were meant to find effective pharmaceutical interventions for infections. To do this, they first needed to deliberately infect the prisoners and the women. This entailed wounding them then through an incision, and then, with the use of bacteria mixtures from the Waffen SS Institute of Hygiene, they rubbed staphylococci, gas bacilli, among others on the wounds, closed the wounds by sewing them, and then dressed up the wound with a cotton-wool filled plaster cast¹⁸. After several deliberations and dissatisfaction with the level of infection (i.e., that the subjects were not sufficiently infected), letter exchanges with the Waffen SS Institute of Hygiene, and the deliberation of these matters in a conference held at Hohenlychen, the lead doctors decided to introduce some changes that would guarantee satisfaction¹⁸. This was the incorporation of wood and glass splinters on top of germs in the concoction. Thus, germs plus glass and/or wood splinters were introduced into the incisions¹⁸. Thus, the Polish women (this time, the 15 prisoners were not anymore part of the experiment) were divided into three groups: those with bacteria plus glass splinters, those with bacteria plus wood splinters, and those with bacteria plus glass and wood splinters. This set-up was “better” for the Nazi scientists as these conditions were more similar to those encountered by the soldiers on the battlefield.

Still, the scientists wanted the wounds to be as similar to battle wounds as possible. They initially thought about inflicting wounds by using firearms, i.e., by inflicting the women with real gunshot wounds, but for some reason they decided against this.

Instead, they made changes on how incisions are made to simulate gunshot wounds: they tied up the blood vessels on both sides of the wound to stop circulation¹⁸. With these “methodological” revisions, the scientists did two series, the first one without the use of glass or wood splinters. For each stage, the scientists waited until the wounds reached a specific infection rate before patients were provided with sulfanilamide drugs. They also had two women as control, i.e., women who had incisions but were not provided any medical intervention.

Aside from pharmaceutical interventions, the Nazi scientists also did muscle, nerve, and bone transplant experiments on the same group of Polish women. The goal of the experiments was to understand the regenerative processes of bones, muscles, and nerves. In these experiments, the women’s bones, muscles, and nerves were broken up, dissected, and grafted¹⁸. Needless to say, the pain was unbearable, especially when anesthetizing the subjects was not a priority. The subjects were also repeatedly victimized as they were subjected to several of these surgical experiments¹⁸.

Nerve operations consisted of removing parts of the lower limbs¹⁸ while bone experiments included bone breaking, bone grafting, and bone splitting. In some cases, bones from the lower limbs were broken and then re-set with a cast. It was common practice that the cast was removed before the bone can fully heal since the goal was to understand regenerative processes.

Part of the experiment were bone transplants. This consisted of removing the left and the right tibia and then grafting them on the opposite leg (thus, the left tibia will be grafted on the right leg and vice-versa), but also the removal of the fibula and then grafting it on the tibia. They would also remove parts of the fibula altogether. There were also other sections of the experiment where incisions to the tibia were made in the first operation after which splinters were removed on the second operation. It was said that one operation consisted of no less than six incisions¹⁸.

Of the 74 women, 5 died because of the experiments, 6 were executed and 63 of them survived¹⁹.

Tuberculosis experiment: This was the infamous experiment by Dr. Kurt Heissmeyer that victimized 30 Russian prisoners and 20 children^{15,20}. There was also documentation that around 200 adults died from these experiments¹⁵, though how many in total were subjects remains unknown.

The experiments were held at the Neuengamme concentration camp. The hypothesis of the experiment was that the injection of live tuberculosis bacilli would create an immune response and thereby act as a vaccine against tuberculosis²⁰. Also, Heissmeyer posited that “only an “exhaustive” organism was receptive to such infection, most of all the racially “inferior organism of the Jews””¹⁵, a clearly pseudo-scientific and racist hypothesis. Thus, Heissmeyer proceeded to inject live tuberculosis bacilli into the lungs of the subjects and removed lymph glands from the arms of the 20 children. As mentioned above, 200 adults died because of these experiments. Of the Russians, 4 were hanged and then dissected. All the 20 children plus their caretakers were hanged at Bullenhauser Dam in an attempt to hide the experiments from the Allied forces¹⁵.

Wound experiments: the death of soldiers due to hemorrhage was common, so the development of a blood coagulant that soldiers can administer and use was needed. As such, Himmler ordered Dr. Sigmund Rascher to do an experiment on the latter’s coagulant^{15,16}. The experiment was held at Dachau concentration camp. He hypothesized that his coagulant (composed of beet and apple pectin) would reduce bleeding from gunshot wounds. To test, he would shoot prisoners in the spleen, neck, chest, or limbs after administering his coagulant. He also amputated some of the subjects for the same purpose.

Infertility experiments: The gynecologist Dr. Carl Clauberg initiated these experiments with the authorization of the SS Chief Heinrich Himmler. The intention of the experiment is to cause infertility on a mass scale, i.e., “to create a “negative demography” among the “Eastern Peoples” in the areas that had already been conquered during the war”²¹. The experiments were held at Auschwitz and at Ravensbrück. Around 700 women, mostly Jewish, were the subjects of the experiments. The experiments consisted of Clauberg injecting his concoction into the fallopian tubes of the women, which caused severe inflammation, severe pain, and sometimes death^{21,22}. He also extended experiments on men which consisted of subjecting their testicles to large doses of radiation and eventually castrating them^{21,22}.

Twin experiments: The experiments on twins, dwarfs, and people with physical abnormalities by Dr. Joseph Mengele were probably the most famous of all the infamous Nazi experiments. His experiments were varied and our intent here is simply to provide snippets of his massive experiments. Mengele was particularly interested in this demographic and it is quite easy to see why. The Nazi ideology of a superior race held anything that is outside its model of the perfect Caucasian as aberrant and unwanted.

This was the case of dwarfs and individuals with physical abnormalities. The twins, on the other hand, was interesting because unlocking its secrets could be the key to the multiplication of the “Aryan race”^{13,15,23}.

For his experiments, Mengele received a grant from the German Research Foundation. He used his grant to build a pathology laboratory in Auschwitz. For the experiment on twins, around 1000 pairs were used, of which around 200 pairs survived¹⁵. The twins were originally from Central and Eastern Europe, i.e., from Romania, Hungary, Czechoslovakia, and Poland. Most were Jewish, though some were Sinti and Roma¹⁴.

Mengele was a very good manipulator. He would present himself as the friendly uncle to the children only to mercilessly exploit and kill them. Included in his “experiments” were amputation of healthy limbs, infection of diseases, unnecessary blood transfusions, and even sewing twins in an attempt to create conjoined twins²³. At one time, Mengele killed 14 twins in one night by injecting their hearts with chloroform and then dissected them. Those that did not die were killed also for the purposes of dissection.

Mengele was also famous for his eye experiments where he attempted to change eye color by directly injecting dye to the eyes of the victims. He also killed and extracted the eyes of individuals with heterochromatic eyes and sent the eyes to Berlin for study^{14,23}.

These accounts of Nazi experiments is not in any way systematic since our goal is simply to provide a sample of the Nazi unethical experiments, which prompted the Nuremberg Trials and eventually the Nuremberg Code of Ethics. We will go back to this point later in this module. For the meantime, let us have a look at another set of unethical experiments, this time from the Orient.

1.3.2 Experiments from Imperial Japan during WW2

Imperial Japan, just like Nazi Germany, is guilty of gruesome and inhumane experiments. The only difference is, Nazi Germany had the Nuremberg trials that included and indicted at least a few of the SS doctors but Imperial Japanese doctors were spared because of an immunity agreement with the USA²⁴.

Shiro Ishii was the director of the infamous Unit 731²⁵, a “covert biological and chemical warfare research and development unit of the Imperial Japanese Army that undertook lethal human experimentation” during WW2.²⁶ The subjects of the various experiments were varied as well. Victims included “common criminals, captured bandits, anti-

Japanese partisans, political prisoners, the homeless and mentally handicapped, and also people rounded up by the Kempeitai military police for alleged “suspicious activities.” They included infants, men, the elderly, and pregnant women”²⁶. Just like the Nazi experiments, experiments from Imperial Japan were meant to understand diseases especially those suffered by soldiers and to find therapies. At the same time, Imperial Japanese experiments also included the intention of developing biological and chemical weapons²⁴. Below are some examples of experiments.

Bacteriological studies: several bacteriological studies were held at Unit 731. Examples would be the experiments by the Surgeon General Masaji Kitano, Surgeon Lieutenant Colonel Naeo Ikeda and Dr. Kameo Tasaki of Manchuria Medical College. Kitano’s experiment entailed the injection of hemorrhagic fever pathogens to subjects, which they attempted to hide as “apes”. One of the research associates, Shiro Kasahara, wrote:

We made an emulsion with 203 ground-up North Manchuria mites and salt water, and injected it into the thigh of an ape hypodermically. This first ape became feverish with a temperature of 39.4 degrees Celsius on the 19th day after injection and moderately infected. Then we took blood of this feverish ape and injected it into the second ape, which became feverish and produced protein in its urine. Typical epidemic hemorrhagic kidney was found at its autopsy...Epidemic hemorrhagic kidney was never found at autopsy in the most feverish period... But kidney, liver, and spleen of this period are most infective²⁴.

After injecting the ground up mites on salt water into the first subject and then injecting blood samples from the infected subject to another subject, they vivisected the subjects possibly while they were still alive.

Ikeda’s experiment was similar to Kitano’s. Ikeda’s experiment was basically to see how infectious hemorrhagic fever was. It consisted of taking blood from a feverish patient and injecting this blood to healthy subjects.

Tasaki, a research associate of the Department of Dermatology and Urology of Manchuria Medical College, on the other hand, did a human experiment on lymphogranuloma²⁴. Tasaki made an emulsion from the grated brain of an infected mouse and injected this emulsion into the prepuce of a “guerrilla”²⁴. A papula grew because of the injection. This subject was then executed two weeks after the injection²⁴.

Physiological studies: just like the SS doctors, doctors from the Imperial Army also did their freezing experiments. Hisato Yoshimura's experiment was an example. According to a witness:

I saw experiments performed on living people for the first time in December 1940. I was shown these experiments by researcher Yoshimura, a member of the 1st Division. These experiments were performed in the prison laboratory. When I walked into the prison laboratory, five Chinese experimentees were sitting on a long form [bench]; two of these Chinese had no fingers at all, their hands were black; in those of three others the bones were visible. They had fingers, but they were only bones. Yoshimura told me that this was the result of freezing experiments²⁴.

In another experiment, two naked men were put into a 40-50 degree below zero environment and were observed and filmed until they died. Needless to say, these men suffered a terribly agonizing death.

Yet in another experiment, Imperial doctors wanted to know how long human beings can live only on plain water and distilled water. Dr. Satoshi Sugawara experimented on 100 subjects that include men, women, children, and infants. According to an assistant,

I was ordered to help civilian Dr. Satoshi Sugawara's experiment to learn how long man can live only on distilled water. The subject lived for 45 days with ordinary water and 33 days with distilled water. A subject forced to drink distilled water asked me, "Mister, please give me tasty water." The subject who lived for 45 days was a physician called Zuo Guangya, a very intelligent man, not a bandit²⁴.

Therapy development experiments: Unit 731 also had several vaccine experiments. One of those were Surgeon Major Masahiko's plague vaccine experiment. According to a junior assistant, the experiment went as follows:

Unit 731 was developing an envelope vaccine of plague . . . Karasawa Division, to which I belonged, also performed human experimentation and vivisection on five Chinese under the pretext of a virulence test of the germ. First we collected blood from them and measured their immunity. On the next day, we injected four kinds of plague vaccines to each of four subjects. No vaccine was given to one subject as control. A week later, vaccines were given again. A month later, we injected 1.0 cc liquid with the same number of plague germs in every subject. All five were infected

with plague. . . . The man that had no vaccine was infected first. Two or three days later he became feverish and pale. On the next day he was dying and his face grew darker. He was still alive but the members of the Special Division, which administered the special prison of “Maruta” [“logs”] brought him naked on the stretcher to the dissection room where we awaited him. . . . Lieutenant Hosoda auscultated his heartbeat on his chest. At the moment the auscultation finished, Surgeon Colonel Ohyama ordered “Let’s begin!”²⁴

There were also experiments on vaccines against cholera that were led by Dr. Yamaguchi. In this experiment, 20 Chinese prisoners were grouped into three arms: one group were given a vaccine made with ultrasonic devices, the other arm was provided a vaccine made at an Army College, and another group was the control and therefore did not receive any intervention. After receiving vaccines, all subjects were made to drink cholera-contaminated milk. All the members of the control group died but because the vaccines proved effective, Ishii ordered Yamaguchi to produce ultrasound-attenuated vaccine on a large scale²⁴.

Biological weapons experiment: According to one US investigator, human subjects were used to test anthrax bombs:

In most cases the human subjects were tied to stakes and protected with helmets and body armor. The bombs of various types were exploded either statically, or with time fuses after being dropped from aircraft. . . . The Japanese were not satisfied with the field trials with anthrax. However, in one trial with 15 subjects, 8 were killed as a result of wounds from the bombs, and 4 were infected by bomb fragments (3 of these 4 subjects died). In another trial with a more efficient bomb (“Uji”), 6 of 10 subjects developed a definite bacteremia, and 4 of these were considered to have been infected by the respiratory route; all four of these latter subjects died. However, these four subjects were only 25 meters from the nearest of the 9 bombs that were exploded in a volley.

Finding information about the gruesome experiments by Imperial Japan is much more complicated and difficult than that of Nazi Germany, partly because of the immunity agreement with the USA. As with the Nazi Germany experiments, the Japanese experiments were also grave violations of human rights, not only in terms of lack of informed consent, but in terms of treating human subjects as disposable experimental entities. Judging by how the experiments exposed human participants to grave danger

and even intentional death, all of these experiments would still be considered unethical, even if “consent” was secured. For pictures, documents, and accounts of these experiments, visit [Pacific Atrocities Education](#).

1.3.3 The Nuremberg Code

After WW2, and because of the Nuremberg Trial against some of the Nazi leaders and doctors, the Nuremberg Code for research was drafted. Though the Code is a direct reaction against the Nazi experiments, it is quite easy to see how the code is very relevant for the Imperial Japanese experiments as well. The Code states the following:

1. The voluntary consent of the human subject is absolutely essential.
2. The experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods or means of study, and not random and unnecessary in nature.
3. The experiment should be so designed and based on the results of animal experimentation and a knowledge of the natural history of the disease or other problem under study that the anticipated results will justify the performance of the experiment.
4. The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury.
5. No experiment should be conducted where there is an a priori reason to believe that death or disabling injury will occur; except, perhaps, in those experiments where the experimental physicians also serve as subjects.
6. The degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment.
7. Proper preparations should be made and adequate facilities provided to protect the experimental subject against even remote possibilities of injury, disability, or death.

8. The experiment should be conducted only by scientifically qualified persons. The highest degree of skill and care should be required through all stages of the experiment of those who conduct or engage in the experiment.
9. During the course of the experiment the human subject should be at liberty to bring the experiment to an end if he has reached the physical or mental state where continuation of the experiment seems to him to be impossible.
10. During the course of the experiment the scientist in charge must be prepared to terminate the experiment at any stage, if he has probably cause to believe, in the exercise of the good faith, superior skill and careful judgment required of him that a continuation of the experiment is likely to result in injury, disability, or death to the experimental subject²⁷.

1.3.4 Tuskegee Syphilis Study

The last case we will look at is the infamous “Tuskegee Study of Untreated Syphilis in the Negro Male” (full title of the study), which was conducted by the United States Public Health Service (USPHS) in 1932 and ended in 1972²⁸. The subjects were 600 African American men from Macon County, Alabama. Most if not all of these men were sharecroppers²⁹. The study was meant to understand the natural progression of syphilis. The study involved blood tests, x-rays, spinal taps, and autopsies of the subjects²⁸.

The study started by recruiting participants on the pretense that it was treatment. The announcement read:

Colored people, do you have bad blood? Free Blood Tests, Free Treatment by Country Health Department and Government Doctors. You may feel well and still have bad blood. Come and bring your family³⁰.

Bad blood is a generic term commonly used within the African American community to refer to “a host of diagnosable ailments including but not limited to anemia, fatigue, and syphilis”²⁹. Since they promised “treatment,” there needed to be deception in the form of ineffective “medicine”, i.e., ointments or capsules with too small doses of neoarsphenamine or mercury²⁸. To make sure that patients do not drop out, they provided free rides for medical appointments, gave out hot meals, and delivered the “medicines” to the subjects. They also covered funeral expenses, which allowed the medical team to autopsy the subjects²⁸.

Aside from deception, the USPHS also actively made sure that the patients did not receive treatment. They, for example, provided county doctors with the list of the participants so as not to treat these participants. They also provided the same list to the Alabama Health Department for the same purpose. Then, in 1941, they ensured that the men were removed from military draft as required health checks would discover syphilis, which would then mean the provision of treatment²⁸.

The study continued even beyond 1947 when penicillin became the standard treatment of syphilis and when the USPHS established Rapid Treatment Centers that treated syphilis with the new antibiotic. Because of the study's goal, the study subjects were not provided with penicillin. It was only in 1972, at the end of the study, did the public know about the study through a newspaper piece stating the end of the study. By this time, only 74 of the test subjects were still alive²⁸. "Largely in response to the Tuskegee study, Congress passed the National Research Act in 1974, and the Office for Human Research Protections was established within the USPHS. Obtaining informed consent from all study participants became required for all research on humans, with this process overseen by Institutional Review Boards (IRBs) within academia and hospitals"²⁸.

1.3.5 The Belmont Report

Largely as a reaction to the Tuskegee Syphilis Study, the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research deliberated on research ethics and its principles in 1976 and drafted what is now known as the Belmont Report. The Belmont Report is the precursor of the four principles of bioethics by Beauchamp and Childress as it expounded on the principles of respect for persons, beneficence, and justice as foundations of informed consent, assessment of risks and benefits, and fair subject selection. The full Belmont Report may be found here: <https://www.hhs.gov/ohrp/regulations-and-policy/belmont-report/read-the-belmont-report/index.html#xbasic>

1.4 Conclusion

In this module, we established the foundational concepts of research and research ethics, emphasizing the value of research for advancing healthcare while recognizing the ethical tensions inherent in involving human participants. We explored various knowledge production modes, each with its own methodological and epistemological orientation, but all requiring rigorous ethical oversight when human beings are involved. Through historical reflection, we demonstrated how grievous abuses in the name of

research—such as those committed by Nazi Germany, Imperial Japan, and the United States during the Tuskegee Syphilis Study—have shaped today’s ethical frameworks, including the Nuremberg Code, the Declaration of Helsinki, and the Belmont Report.

These historical and conceptual insights underscore the indispensable role of RECs in upholding the dignity, rights, and welfare of research participants. As custodians of ethical research, REC members are tasked not only with identifying procedural compliance, but also with engaging in nuanced ethical deliberation informed by facts, principles, and moral reasoning. This module thus lays the groundwork for deeper engagement with ethical principles, theories, and deliberative tools that will be discussed in subsequent modules of this Manual.

Note: REFERENCE LIST at the end of Module 2.

2 **Module 2:** Ethical Principles and Theories of Ethics Applied in Research

SCOPE OF THE MODULE

This module provides an overview of the ethical principles and theories that are foundational to ethical reflection and justification in health-related research. It distinguishes between mid-level ethical principles—such as autonomy, beneficence, non-maleficence, and justice—and higher-level ethical theories, including deontology, teleology (utilitarianism), virtue ethics, and care ethics. Through conceptual clarification and practical examples, the module equips Research Ethics Committee (REC) members with the theoretical tools needed to support ethical deliberation and decision-making. Emphasis is placed on understanding how these tools function within the framework of Reflective Equilibrium, preparing REC members to evaluate research protocols with clarity, coherence, and ethical depth.

LEARNING OBJECTIVES:

By the end of this module, REC members should be able to:

- Distinguish between ethical principles and ethical theories, and understand their respective roles in ethical justification.
- Explain and apply the four core biomedical principles—autonomy, beneficence, non-maleficence, and justice—in research ethics review.
- Describe and differentiate major ethical theories, including deontological, teleological, virtue-based, and care-based ethics.
- Reflect on how different ethical frameworks influence protocol evaluation and risk-benefit assessments in research involving human participants.
- Apply ethical principles and theories as part of a Reflective Equilibrium approach to ethical deliberation.

In Module 1, we briefly introduced Reflective Equilibrium as a method of ethical justification, emphasizing that it involves a reasoned balancing of ethical principles or theories, moral intuitions, and relevant facts. This module now focuses on the first of these components: ethical principles and theories. As a branch of applied ethics, research ethics draws heavily on the tools of normative ethical analysis. It is therefore essential that members of RECs are well-versed in these tools and can competently apply them during ethical deliberation.

2.1 What are ethical principles and theories?

2.1.1 Ethical Principles

The process of ethical reflection and ethical justification requires making ethical principles and/or theories explicit. These form part of the aspects that the decision maker, in this sense the REC members, would have to balance given the facts and personal moral intuitions. Principles are distinct from ethical theories since principles are mid-level rules or norms reflective of action-guiding criteria set/accepted by the relevant community (in this case, the research community) as constitutive of the latter's values. Ethical principles are “mid-level” in the sense that they are in between the “low-level” concrete decisions in particular situations and the “high-level” ethical theories. Examples of ethical principles are the four biomedical ethical principles elaborated by Beauchamp and Childress in the multiple editions of the book, *Principles of Biomedical Ethics*⁸: autonomy, beneficence, non-maleficence, justice. There have been challenges on these four principles, not only in terms of the completeness of the principles, but also because of claims of the approach's limitations in terms of cultural sensitivity, conflict resolution, over-simplification, applicability to vulnerability, among others.^{31–35} Those who are interested in these challenges are invited to go through the references. For our purposes, we will look at the four principles of Beauchamp and Childress and relate them to some practical examples.

Autonomy refers to the principle acknowledging self-governance. This principle requires two conditions: “liberty (independence from controlling influences) and agency (capacity for intentional action).”⁸ This is the principle that underlies the practice of informed consent. Researchers ask for the participants' consent and we do so in a manner that truly informs them because, as human beings, research participants are self-governing. They have an inherent right to make decisions for themselves. In the absence of one or both of the conditions of autonomy, for example in the case of young children who does not have the agency yet to decide, then consent takes the form of “presumed consent” where the parents, as the decision makers, do so in the best interest of the child and with the assumption that their decision is such that the child, when grown up as a reasonable adult, will consent to participation in the research in question. The same may be said for other individuals who may be agency-challenged.

Beneficence is the principle that “refers to a statement of general moral obligation to act for the benefit of others.”⁸ It may be summarized by the phrase, “do good.” In medical research, this may refer to ensuring that research participants, the community, and/or society benefit from the practice or fruits of research. This underlies the practice of sharing of results and interventions, otherwise known as benefit-sharing (however, as we shall see shortly, decisions of benefit-sharing may also be an issue of justice). This is also the foundation for the social value of research, i.e., that the research is made with the assumption that it can potentially benefit science and society.

Non-maleficence is the principle requiring us to not harm others summarized by the statement, “first, do no harm.”⁸ In research, researchers are required to avoid and/or minimize risks and harms to research participants and the community in all research-related procedures. This means, for example, reviewing protocols for excessive demands on the research participants (for example, requiring participants to be on a medical device for prolonged hours or exposing participants to high-risk interventions) and minimizing these risks through the use of risk-mitigation measures such as dose escalation and monitoring, built-in stopping rules, and carefully crafted exclusion criteria.

Justice is the principle that centers on fairness in the distribution of the benefits and burdens of healthcare. This principle underlies the requirements for *fair* subject selection (that research participants are chosen because of the requirements of science and not because of convenience); equitable access to research results (e.g., discussions on post-trial access, i.e., if and how participants and/or community or society should *equitably* benefit after a clinical trial); inclusion of underrepresented groups; fair distribution of risks and burdens; allocation of scarce resources; and advancing health equity.

2.1.2 Ethical Theories

Ethical theories, on the other hand, are philosophical frameworks for ethical judgment meant to guide the reflection on rightness or wrongness of a decision and/or an act. Such theories have been traditionally categorized as deontological or teleological, though there have been challenges on these broad categorizations. Below we explicate these two large categories and provide some examples. We also provide an example of an ethical theory that does not fit squarely into these two broad categories, i.e., Care Ethics. Note that there are numerous ethical theories and we only cover a fraction of them in this Module.

Ethical theories that fall within the category of **Deontological Ethics**^{8,36} are grounded in the idea that certain actions are morally obligatory, regardless of their consequences. The core focus of such theories is *duty and obligations*, guided by the key question: *Is this action inherently right or wrong?* As such, ethical judgment is/ought to be based on the intrinsic rightness of actions, which are typically derived from universal moral laws or principles. The most common example of Deontological Ethics is Kantian Ethics (as originally articulated by the Enlightenment philosopher, Immanuel Kant). In medical research ethics, deontological reasoning provides philosophical foundations for respecting the autonomy and rights of participants, independent of the foreseen scientific benefits of research. Concretely, this may mean, for example, requiring informed consent even though this would require extra effort from the researcher and opposing deception or coercion, even if these might lead to beneficial outcomes. In both

instances, research participants ought to be respected as ends and never solely as means.

Teleological Ethics^{8,36}, particularly utilitarianism, evaluates the morality of an action based on its outcomes or consequences. It asks the key question: *Does this action maximize benefits and minimize harms?* Ethical judgment is based on utility, i.e., a unit of good defined by the decision-maker and that which should be maximized. Opposite to utils would be disutility which should be minimized. An action is considered good if it results in more utility than disutility. This approach is highly influential in medical research ethics when, for example, RECs assess the risks and the benefits of a study, when determining and weighing resource allocation, and deliberating on public health impacts. For example, teleological reasoning may support conducting a high-risk clinical trial if the potential results could lead to significant population-level health improvements. However, such reasoning must still be balanced with safeguards to individual participants, especially since such safeguards may increase utility over disutility.

Another example of teleological ethics is Virtue Ethics. **Virtue Ethics**³⁷ centres on the moral character of the individual rather than specific actions or outcomes. It is teleological ethics because all its claims and norms are for one purpose/end: human flourishing (eudaimonia). Its guiding question is, “*What kind of person should I be?*” and “*What would a virtuous person do?*” The theory focuses on the cultivation of virtues (defined as good habits) such as honesty, courage, integrity, and compassion since these good habits enable a person to live a life of human flourishing. In medical research, virtue ethics emphasizes the importance of a research culture marked by virtues such as trustworthiness, humility, equity, solidarity, among others. A virtuous researcher is someone who habitually, i.e., consistently and with ease, acts with integrity, irrelevant whether someone is watching or not.

An ethical theory that cannot be categorized as simply deontological or simply teleological is Care Ethics. **Care Ethics**³⁸ offers a relational and context-sensitive approach to morality. It emphasizes empathy, attentiveness, and the responsibilities inherent in human relationships. Its guiding question is, *What does caring demand in this specific situation?* In this sense, ethical judgment is based on responsiveness to the needs of others. In medical research, “others” may refer to research participants, to vulnerable populations, or the community. This approach is especially valuable in highlighting the relational duties of researchers toward participants and highlights responsibilities such as listening attentively to the participants’ concerns, being responsive to power imbalances, and maintaining ongoing ethical engagement beyond formal compliance.

2.2 Conclusion

This module has provided an overview of key ethical principles and theories that guide ethical reflection and justification in health-related research. Ethical principles serve as mid-level action-guiding norms that reflect the values of the research community and inform day-to-day decision-making. Ethical theories, by contrast, offer deeper philosophical foundations for moral judgment and help explain why certain actions or principles are considered ethically justified. Understanding the distinctions and interrelations among these tools equips REC members to engage in more coherent and well-grounded ethical deliberation.

Equipped with these conceptual tools, REC members can better navigate complex ethical dilemmas by applying principles in light of ethical theory, moral intuitions, and relevant facts. Whether justifying the necessity of informed consent (deontology), balancing societal benefits and individual risks (teleology), fostering trust and moral character (virtue ethics), or responding to relational and contextual needs (care ethics), each ethical lens enriches the deliberative process. In the next modules, we will turn to the operational role of RECs and examine how these ethical tools are applied in practice during protocol review and decision-making.

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3 Module 3: The Role and Function of RECs

SCOPE OF THE MODULE

This module equips learners with the necessary skills to effectively operationalize REC functions and demonstrate the capacity to design and follow standard operating procedures (SOPs) and institutional policies and procedures. It covers the fundamental principles and practical aspects of RECs, including their definition, purpose, roles, expertise, and processes for ethical research practices. The module provides a comprehensive understanding of RECs' role in promoting ethical research conduct and participant protection.

LEARNING OBJECTIVES

At the end of this module, the learners will be able to:

- Explain the fundamental principles and purpose of Research Ethics Committees (RECs) and their role in protecting human research participants.
- Describe the composition and expertise typically found within RECs and explain how this diversity contributes to effective ethical review of research.
- Outline the typical processes and procedures followed by RECs in the review, approval, and monitoring of research.

3.1 Definition and Purpose of RECs

3.1.1 Definition of RECs

RECs are specialized committees set up by an organization or research institution to safeguard the rights and welfare of human subjects. The RECs are independent, multidisciplinary groups responsible for reviewing and overseeing research involving human participants to ensure ethical conduct and participant protection. The RECs play a crucial role in protecting the rights and welfare of human subjects involved in research. Without proper oversight from RECs, researchers may not adequately address potential risks or obtain informed consent from participants. RECs ensure ethical standards are met in human subject studies, overseeing the start and follow-up activities. They have the power to mandate changes to research procedures, accept, reject, or terminate investigations, and may also establish guidelines or voice opinions on current research ethics concerns.

3.1.2 Purpose of RECs

The RECs are independent reviewers of research protocols; they ensure ethical and scientific conduct of research, and that participant's rights, safety, and welfare are not violated. The RECs review the science and ethics of the research protocols, and all relevant documentation related to the study to promote high ethical standards in research. RECs have a special responsibility to determine whether the objectives of a research study are responsive to the needs and priorities of the proposed target population in general. By carefully reviewing research protocols, informed consent documents, and potential risks to participants, RECs help to safeguard the well-being of those involved in research studies. Through their commitment to upholding ethical standards, RECs play a vital role in maintaining public trust in the scientific research process.

3.2 Roles and Responsibilities of RECs

Reviewing research proposals. It entails evaluating proposed research for ethical acceptability, ensuring scientific soundness, minimizing risks, and ensuring informed consent procedures are robust. The process of conducting a thorough ethical review of proposals involves:

3.2.1 Maintain Ethical Standards

The proposal review process upholds participant autonomy, encouraging open dialogue and feedback without fear of judgment. Decisions are made collaboratively, considering all perspectives, with no coercion or undue influence. Information comprehension, protection, dignity, privacy, and confidentiality issues are ensured, ensuring a thorough and fair evaluation process that includes the protection of vulnerable populations and fair distribution of benefits and burdens.

3.2.2 Preserve Participants' Rights

Research participants' protection is crucial, ensuring their rights and welfare at all times. While research is essential for human progress, it can sometimes compromise researchers' ability to respect participant rights. This commitment should be made before, during, and after post-study, not just at the initial review. Researchers must actively seek informed consent from participants, ensuring they understand the risks and benefits of the study before agreeing to participate. During the study, researchers must continuously monitor participants' well-being and address any concerns

promptly. After the study is complete, researchers must provide participants with a debriefing and any necessary follow-up care to ensure their rights and welfare are upheld throughout the entire research process.

3.2.3 Monitoring ongoing research

It involves overseeing the conduct of approved research, reviewing progress reports, and addressing any ethical concerns that may arise. The REC must ensure compliance with approved protocols and regulatory requirements, including auditing and monitoring plans. Common issues to monitor include approvals, licenses, documentation, reportable events, participant rights, facility/site issues, safety, unapproved studies, lack of guidelines, Standard Operating Procedures (SOPs), training, and protocol violations and deviations. To effectively monitor these issues, the REC must conduct regular audits and reviews of all research activities. Any deficiencies or non-compliance that are identified must be promptly addressed and remedied to ensure the safety and well-being of all participants involved in the research. By maintaining a thorough monitoring system, the REC can uphold the ethical standards and integrity of the research being conducted.

The monitoring of research studies can be conducted in two ways; On site: This is monitoring performed at the research site. This can only be done physically. Off-site: This is the monitoring of studies away from the research site. This can be done virtually or remotely and is where monitors do not visit the site to review the data and related documents but instead, the monitoring is done virtually. With the use of digital technology, this can be done from wherever the monitors are located. The REC reviews studies through different data sources including annual progress reports, ethics approvals, monitoring reports, serious adverse events (SAEs) reports, adverse events (AEs), suspected unexpected serious adverse reactions (SUSARs) reports, amendments, and de-identified research participants' documents. Consideration must be made to ensure the privacy and confidentiality of participants.

3.2.4 Providing education and guidance to researchers and the community

The REC provides education and guidance on research ethics to researchers and the community, fostering transparency and accountability in research practices through collaborations and ongoing updates to ethical guidelines in response to new

technologies and social issues. By offering workshops, seminars, and resources, the committee ensures that researchers understand and adhere to ethical standards in their studies. In doing so, they promote a culture of integrity and respect within the research community, ultimately enhancing the quality and credibility of research findings.

3.2.5 Facilitating public dialogue on ethical issues

Engaging with the community on research ethics concerns and fostering transparency in research practices. The community must trust the REC's ability to safeguard participants' rights and welfare, and the REC must be confident in its ability to execute its mandate effectively. The REC needs to enhance its capacity to handle ethical issues through continuous training, networking, discussions, and mentorship. By establishing strong relationships with stakeholders and ensuring transparency in its decision-making processes, the REC can build credibility and earn the community's trust.

3.3 Composition and Expertise of RECs

3.3.1 Multidisciplinary Membership

The multi-disciplinary membership of RECs is essential in ensuring a comprehensive review of research proposals. By including individuals from diverse backgrounds such as healthcare professionals, legal experts, ethicists, and community representatives. The RECs can offer a variety of perspectives and expertise. This ensures that research proposals are thoroughly evaluated from various angles, considering the scientific and ethical implications and the potential impact on society and individuals. The multidisciplinary approach helps to uphold ethical standards and protect the rights and welfare of research participants. For example, a research proposal for a new medical treatment undergoes a thorough assessment by medical professionals, legal experts, ethicists, and community representatives to ensure its scientific validity, regulatory compliance, ethical implications, and public opinion. This process ensures responsible and ethical conduct, identifying potential risks and issues, and ensuring the study's ethical and responsible conduct.

RECs should not solely consist of scientific experts, as non-scientific members can identify risks and benefits related to social, legal, or cultural factors. Identifying these

risks and benefits requires value judgments and scientific analysis. A diversity of backgrounds and qualifications, including medicine, law, and social sciences, can prevent biases. Social diversity and gender balance should also be reflected in the committee's composition. Membership should be designed to minimize the potential impact of conflicts of interest on the decision-making process. For example, Institutional RECs require members not affiliated with the institution, while government-sponsored committees should have members not employed by the government. Members with a conflict of interest in a study should not participate in the review of the research.

3.3.2 Lay Membership

Lay Membership in RECs is crucial for ensuring a diversity of perspectives and experiences are represented in the decision-making process. By including individuals who are not necessarily experts in the field, but who bring their unique insights and values to the table, RECs can more effectively evaluate the ethical implications of proposed studies. The lay members help bridge the gap between researchers and the general public, ensuring that ethical considerations are not overlooked or dismissed in pursuit of scientific advancements. Ultimately, the inclusion of lay members in RECs strengthens the overall integrity and accountability of the research process.

The RECs need diverse community representation to understand local attitudes and practices. In some societies, it may be inappropriate to ask people about research without first speaking with community leaders. The committee can evaluate information provided to potential participants through the informed-consent process, incorporating input from the community.

3.3.3 Gender Balance

Gender balance in RECs is essential for ensuring diverse perspectives are considered in decision-making processes. A balanced committee with male and female members can identify biases and prejudices, leading to more ethical and inclusive research practices. Social diversity and gender balance should be reflected in the committee's composition, allowing for a wide range of perspectives and experiences to be considered. This can result in more innovative solutions and a better understanding of different viewpoints, as well as a better representation of the diverse population it serves.

The RECs are essential in reducing gender prejudice in research by incorporating gender aspects into health research. They must be aware of intersectional gender dynamics, biases, and their ethical implications. By considering gender in research, RECs prevent harmful stereotypes and biases. Promoting diversity and inclusivity in research practices can lead to more equitable health outcomes. Their vigilance in addressing gender prejudice is crucial for ethical and responsible scientific practices.

3.3.4 External Expertise

RECs must have expertise and diversity to understand study procedures and potential consequences for participants. Members must be qualified by experience, expertise, and cultural backgrounds, considering gender, cultural backgrounds, and sensitivity to social issues. Each REC should include at least one member with primary concerns in scientific and non-scientific areas, and at least one layperson from the community. Supplementing consultants in specialties can help ensure a comprehensive approach to research ethics.

RECs can enhance their decision-making process by collaborating with external experts. This collaboration offers valuable insights and perspectives, ensuring responsible and thorough research. It also promotes participant well-being and study integrity. External expertise can enhance the quality and effectiveness of ethical assessments, handle complex ethical dilemmas, and ensure comprehensive supervision of research procedures. During the review of the protocols external experts provide a wider range of perspectives and this can result in more thorough ethical discussions. Specialists from a range of disciplines can offer distinctive perspectives, improving the committee's capacity to successfully handle ethical issues. Also, understanding the distinction between generalist and specialist skills may expedite hiring procedures and guarantee that committees are prepared to tackle a range of ethical dilemmas. Even in the face of staff changes, this strategy may preserve the integrity and effectiveness of committees.

Case Study

A newly formed company prepared a protocol to prove the health benefits of water processed by an imported machine to HIV-positive patients. They chose a sanitary

engineer as PI and submitted the protocol to the hospital REC. Since the investigational product was water, REC approved the protocol and ICF immediately.

Source: FERCAP/SIDCER Handbook of Case Studies on Ethical Issues in Health Research

Points for Discussion

1. What are the GCP issues related to the case study?
2. What is the role of the sponsor, the role of the investigator, and the role of the REC?
3. Was the hasty approval justified?
4. What information should REC require in the protocol? In the ICF?
5. What kind of investigator's expertise does the protocol require?

3.4 REC Processes and Procedures

3.4.1 Appointment and Renewal Process

The appointment and renewal process for REC members is crucial for maintaining ethical standards in research involving human subjects. Typically, these committees are established by research institutions or governmental bodies, ensuring a diverse membership that includes experts in research disciplines, community representatives, and legal advisors. REC members are usually appointed for a specific term, often ranging from one to three years, with the option for renewal based on performance and commitment to ethical principles. This system helps to prevent conflicts of interest and ensure that committee members remain impartial and focused on upholding ethical standards. Regular training and updates on research ethics guidelines are also provided to REC members to ensure they stay informed and equipped to make informed decisions on research proposals.

The following factors should be considered during the appointment or the renewal process of the membership:

1. RECs should consist of a reasonable number of members who collectively have the education, training, skills, and experience to review and evaluate the type of research proposals the committee is most likely to receive.
2. Members should include individuals with relevant scientific expertise (depending on the type of research the REC reviews, this may include experts in behavioural and social sciences, health-care providers, and pharmacologists);

members who have expertise in legal matters, public health, and ethics; and lay people whose primary role is to share their knowledge about the communities from which participants are likely to be drawn.

3. Lay people and other members whose primary background is not in health research involving human participants should be appointed in sufficient numbers to ensure that they feel comfortable voicing their views.
4. To support independence, committee membership should include individuals who are not affiliated with organizations that sponsor, fund, or conduct research reviewed by the REC.
5. All REC members should declare any conflicts of interest, and the REC should ensure that members do not participate in reviewing studies in which they have a conflict of interest.
6. Committees should be large enough to ensure many perspectives in the discussion. Quorum requirements should provide that at least half of the members, including at least one lay member and one non-affiliated member, are present to make decisions about proposed research.

The head of the institution is responsible for ensuring the REC has adequate resources to identify and recruit qualified potential members and ensure the overall diversity of the REC membership (gender, ethnicity, community affiliation, and professional experience) through non-discriminatory selection methods. The REC should maintain a roster of regular and alternate members, along with a file of their credentials, and a roster of qualified consultants for attending meetings as invited. Establishing transparent and impartial procedures for selecting and renewing REC membership is essential for ensuring the integrity and credibility of the committee's decisions. By clearly outlining the criteria for membership and the process for selection, the committee can demonstrate its commitment to upholding ethical standards in research. Additionally, regular reviews and evaluations of committee members can help to identify any conflicts of interest or bias, further strengthening the committee's ability to make fair and unbiased decisions.

3.4.2 Training of REC Members

The rapid development of health sciences has increased the complexity of health and behavioral-related research, necessitating multidisciplinary and transdisciplinary approaches and stricter ethical, regulatory, administrative, and quality standards. RECs

must ensure their members and collaborators have the necessary qualifications, abilities, experience, and knowledge to evaluate and approve research projects. Effective governance of members' qualifications and education will help maintain research standards in terms of scientific and methodological soundness, and ethical, regulatory, and quality compliance at every stage of the research process, from protocol development to dissemination of findings and translation.

The training of REC members significantly enhances the reputation of institutions and the RECs and their research personnel by facilitating future funding, and research opportunities, and promoting career development. Therefore, it is recommended that the following resources be carefully managed and monitored by the REC in line with its mandate and goals.

1. **Expertise and skills:** Put in place mechanisms to ensure that RECs have acquired the necessary expertise and skills to carry out their respective tasks in reviewing and approving research projects, whether in research methods (e.g. clinical, epidemiological, qualitative, or mixed-methods; good clinical/laboratory practices) or research-related disciplines or activities (e.g. research ethics, research integrity, data management, scientific writing, planning, research contracts, administration).
2. **Learning opportunities:** Give all REC members access to adequate learning opportunities, based on their background and tasks continuously.
3. **Training/learning records:** Put in place mechanisms to document the training/learning activities and qualifications of all REC members.
4. **Professional licenses:** Put in place mechanisms to ensure that where necessary, the REC members have the appropriate professional licenses to practice in compliance with national laws and regulations.

Providing comprehensive initial and continuing training to equip REC members with the necessary knowledge and skills is essential for effectively reviewing research proposals and addressing ethical challenges. The training is crucial for their effective responsibilities and understanding of research ethics laws and regulations. This enhances the quality and integrity of the research review process, protecting human subjects. Ongoing training helps REC members stay updated on emerging ethical issues and best practices, enabling the members to make informed decisions and

recommendations. This ensures the protection of human subjects and the integrity of the research review process. Various training programs, including workshops, seminars, online courses, and on-the-job training would be conducted. Ongoing education and professional development opportunities are essential for staying updated on regulations and best practices. Training can impact the efficiency and effectiveness of the research ethics review process. Strategies for evaluating training effectiveness and making improvements based on participant feedback are also discussed.

Every REC member shall undertake at least one course in human research protection within one year of appointment to the REC, and thereafter, should undergo continued research ethics education or training at least once every two years. The REC may, at its discretion, invite individuals with competence in special areas to assist in the review of protocols, which require expertise beyond, or in addition to that available in the REC. However, these individuals do not vote at REC meetings.

The REC members should have refresher training every two years but not limited to the following: Research ethics, Good Clinical Practice (GCP), the relevant laws and regulations, and human subjects' protection. The REC members and staff may exchange ideas, information, and experiences with international institutions and organizations related to research ethics as part of capacity development.

3.4.3 Confidentiality of the REC Committee

The foundation of the patient-physician interaction is the ethical ideal of secrecy, originally stated in the Hippocratic Oath. Even if the dynamic between researchers and study participants differs from that of a typical doctor-patient interaction, maintaining anonymity is still a top priority. Medical ethics emphasize confidentiality to foster trust and allow individuals to disclose sensitive information without fear of public disclosure. This trust is crucial for maintaining public health and preventing untreated illnesses, which can pose a serious threat to others. In many countries, nondisclosure is guaranteed by legislation.

Maintaining strict confidentiality of research proposals and discussions within the REC is crucial for protecting the privacy of researchers and participants. This includes securely storing any sensitive information and only sharing it with authorized

individuals. By upholding confidentiality, the REC can ensure that all parties involved feel comfortable and safe in sharing their ideas and opinions without fear of repercussions. This commitment to confidentiality is essential in promoting trust and integrity within the research community.

Ethics review committees must carefully examine how research-related data will be kept private and make sure that there is as little chance as possible that patients may experience adverse effects because of information exposure. This comprises data discovered following research or data about a person's involvement in a study. Ethics review committees also need to consider how researchers will handle and store the data to minimize the risk of breaches or leaks. Additionally, they must ensure that participants are fully informed about the potential risks of participating in the study and have given their informed consent before any data is collected. Overall, protecting the privacy and well-being of research participants is paramount in conducting ethical research.

During the conduct of the REC activities, members shall be provided with confidential information and documentation. REC members are required to agree to take reasonable measures to protect the confidential information; subject to applicable legislation not to disclose the confidential information to any person; not to use the confidential information for any purpose outside the committee's mandate, and in particular, in a manner which would result in a benefit to the REC member or any third party; and to return all confidential information (including any minutes or notes to the Chairperson upon termination of the functions as a member.

Confidential documents/information include but are not limited to the following; study protocols and related documents including case report forms, study tools, informed consent documents, expert opinions or reviews, and study reports; REC documents including Standard Operating Procedures (SOPs), meeting minutes, recommendations, and decisions; correspondences from; investigators, experts, auditors, National Regulatory Agencies (NRAs), and study participants; copies of all versions of documents, including draft and sequential definitive versions.

3.4.4 Safeguarding Personal Information

The REC must safeguard the personal information of the researchers, study participants, and communities. Personal data, including all data related to an identifiable or identified natural person (the "data subject"), is crucial for protection. This can be done directly or indirectly, using unique characteristics or identification numbers related to physical, physiological, mental, economic, cultural, or social identity. This includes any information that can be used to identify a specific person, such as their name, social security number, address, phone number, and other identifying characteristics; information that indicates that a person belongs to a specific group of people, like the fact that they work in a specific office or reside in a specific apartment building; and a combination of information, such as physical characteristics, birth date, and place of employment, that can be used to identify a specific person. Protecting identifiable information is crucial, especially for sensitive details like medical records, mental health, drug misuse, genetic traits, social status, political affiliation, religious convictions, sexual orientation, and risky behaviours. These details should be carefully considered to avoid stigmatizing illnesses, ensure safety, and maintain public trust.

Finally, the REC should adhere to the procedures when reviewing protocols and communicating with researchers, ensuring compliance with institutional or local regulations. Security measures should be in place for records, including storage in hard copy, electronic, or both formats. Procedures should specify access to committee files and papers, and staff members should receive training on confidentiality, record-keeping, and retrieval.

3.4.5 Accountability to the Appointing Authority and the Public

RECs are responsible for ensuring ethical research conduct, requiring accountability to their appointing authority. This accountability promotes transparency, maintains ethical standards, and builds public trust. Accountability ensures transparency and accountability to the appointing authority and the public, providing regular reports on REC activities and decisions. This reporting process allows for oversight and ensures that the REC is upholding ethical standards in all research activities. By maintaining accountability, the REC can demonstrate its commitment to ethical research conduct and the protection of human subjects. Ultimately, this transparency and accountability

help to safeguard the integrity of the research process and uphold public trust in the scientific community.

The REC should establish procedures for accountability and openness, providing information on ethics review procedures, funding sources, composition, and approved research proposals to the public and institution. Researchers and participants should be allowed to ask questions and receive responses from RECs, promoting transparency and accountability. This transparency not only helps to build trust between researchers, participants, and the REC but also ensures that ethical standards are being met throughout the research process.

The institution head monitors the quality management systems of RECs to ensure ethical standards are followed. Regular audits assess the committees' effectiveness in reviewing proposals and protecting human subjects. Any violations or discrepancies are promptly addressed to maintain the institution's research activities' integrity and credibility. The REC shall provide regular reports to the appointing authority. These reports will detail the progress of ongoing projects, any challenges or obstacles encountered, and recommendations for improvement. The REC will also be responsible for presenting these reports in person to the appointing authority on a quarterly basis or as deemed necessary by the institution. Additionally, the REC will ensure that all relevant stakeholders are kept informed and updated on the activities and outcomes of the projects.

Upholding Institutional Values and Reputation by the REC is essential in ensuring that all research conducted within the institution adheres to ethical standards and guidelines. By upholding these values, the committee helps to maintain the institution's reputation as a trustworthy and responsible research entity. This not only benefits the institution's standing within the academic community but also ensures that research participants are treated fairly and ethically. Ultimately, the REC plays a crucial role in upholding the integrity of the institution and the research it produces.

The REC plays a crucial role in upholding the institution's mission of promoting ethical research practices and ensuring the protection of human subjects. By reviewing research proposals and ensuring that they meet ethical standards, the committee helps to maintain the institution's reputation for conducting responsible and trustworthy

research. Additionally, the committee's oversight can help prevent potential harm to research participants and uphold the institution's commitment to integrity and excellence in research.

The REC should implement several strategies to increase accountability and transparency in the institution, including;

1. **Consultations:** The RECs should be available for consultation with the host institutions on ethical research issues, including policy development, addressing concerns, and providing guidance on emerging challenges, ensuring ethical considerations are addressed. It is important for RECs to be easily accessible and responsive to the needs of researchers and institutions to ensure that ethical standards are upheld throughout the research process. By guiding emerging challenges, RECs can help institutions navigate complex ethical issues and make informed decisions. Ultimately, the goal of consultations is to promote ethical research practices and protect the rights and well-being of research participants.
2. **Efficient Use of Resources:** RECs should utilize resources effectively and efficiently to fulfill their duties. This can include optimizing staffing levels, streamlining processes, and implementing cost-saving measures. By managing resources effectively, RECs can ensure that they can meet the needs of their stakeholders and carry out their mission successfully. Additionally, efficient resource use can help RECs maintain financial stability and sustainability in the long term.
3. **Continuous Improvement:** RECs should strive for continuous improvement in their processes and procedures to enhance their effectiveness and efficiency. This can be achieved through regular evaluations, feedback from stakeholders, and benchmarking against industry standards. By constantly seeking ways to improve, RECs can stay ahead of the curve and remain competitive in the market. Implementing a culture of continuous improvement can also lead to higher levels of researchers' and communities' satisfaction, and loyalty.

4. Communication and Feedback: Establishing clear communication channels with stakeholders and holding public forums to address concerns and gather feedback. These efforts will ensure that all parties involved are informed and engaged in the decision-making process. By actively seeking input and addressing any issues that arise, we can work towards creating solutions that benefit everyone involved. Building trust and fostering open communication will be key to successfully navigating any challenges that may arise. Additionally, the REC should create a whistleblower policy to encourage employees to report any unethical behavior without fear of retaliation.

3.4.6 Methods of Working for the RECs

The RECs are mandated to create detailed guidelines, including policies and procedures, that can help to standardize operations and decision-making processes within the committee, but also ensure transparency and accountability in decision-making. The policies may serve as a foundation for ethical decision-making and operational consistency, and these may include conflict-of-interest policies, data protection policies, and participant protection guidelines. The procedures usually provide step-by-step processes for submitting proposals, reviewing protocols, reporting adverse events, and addressing non-compliance.

The statutes and policies establish explicitly the goals and boundaries for the REC's responsibilities to ensure focused and effective oversight. Clear goals and objectives provide direction, as this ensures the REC's capacity to fulfill its mission of protecting research participants and upholding ethical standards. It also helps specify the type of research the REC reviews, e.g., clinical trials, and its jurisdiction, e.g., institutional, national, or international. Clear goals also help align the REC's work with legal, institutional, and international ethical guidelines.

To ensure a quality management structure, RECs are also involved in the implementation of a structured framework that allows for systematic monitoring and improvement of REC activities. The framework includes roles, responsibilities, and workflows that support systematic monitoring and improvement. This framework also comprises the Quality Assurance (QA) unit that can oversee REC operations, and the documentation systems for tracking submissions, decisions, and follow-ups. The REC statutes and guidelines set forth effective management and quality assurance processes to ensure the ethical conduct of research.

3.4.7 Rules of Procedure

The RECs should have documented procedures for ethics oversight, including application submission, protocol review, research monitoring, document management, meetings, decision-making, and conflict management, covering all aspects of research. These procedures should be clearly outlined in a comprehensive manual that is easily accessible to all members of the REC. All members must be trained in the procedures to ensure consistency and transparency in the ethical review process. Additionally, regular audits should be conducted to ensure compliance with these procedures and to identify any areas for improvement.

The procedures ensure that the rights and welfare of human research participants of such research will be overseen and protected uniformly, regardless of personnel changes. Written procedures must be in place to ensure the highest quality and integrity of the review and oversight of research involving human research participants and for the adequate documentation of such oversight. Standard Operating Procedures (SOPs) provide the framework for the ethical and scientifically sound conduct of human research.

The REC should establish clear criteria for ethical review of human research proposals, including content, supporting documentation, due dates, costs, and review schedule. Templates for documents like information sheets, permission forms, and sample application forms should be available. Screening guidelines should outline a procedure for assessing application completeness and corresponding with incomplete applicants. They should also determine which applications qualify for expedited review or are excluded from REC review.

The REC should have written procedures to ensure ethical decisions are based on national laws and policies. These should cover the scientific design and conduct of research, risks and benefits, study population selection, use of inducements, confidentiality protection, informed consent, and impact on communities. In addition, the REC should also have procedures in place for how to handle conflicts of interest, the involvement of vulnerable populations, and the dissemination of research findings. These procedures must be clearly outlined and followed to maintain the integrity and ethical standards of the research being conducted. By adhering to the procedures, the

REC can ensure that research is being carried out responsibly and ethically, ultimately benefiting both the participants and the scientific community as a whole.

During the conduct of the REC meetings, the members should have sufficient time to review research proposals, receive relevant documents in advance, and have sufficient time to discuss research protocols. They should be familiar with distribution procedures, correspondence, and understanding of current and previous meetings' agendas and minutes, including start and end times and the number of applications discussed. Meetings should be sufficient to allow for full discussion. Members should also be allowed to ask questions, seek clarification, and voice any concerns they may have regarding the research proposals under review. REC meetings need to be structured in a way that allows for thorough evaluation and decision-making, ensuring that all research protocols are thoroughly vetted before approval is given.

3.4.8 Follow-up Mechanisms of Approved Research

Implementing mechanisms for monitoring the progress of approved research and addressing any ethical issues that may emerge during the study is crucial for maintaining the integrity of the research process. Regular check-ins with researchers and participants can help ensure that ethical guidelines are being followed and that any potential issues are addressed promptly. By actively monitoring the progress of approved research and addressing ethical concerns as they arise, researchers can maintain the trust and confidence of both the public and the scientific community. This commitment to ethical research practices is essential for upholding the credibility and validity of scientific findings.

The REC must establish procedures for the concurrent monitoring of research activities involving human research participants. A periodic review of research activities is necessary to determine whether approval should be continued or withdrawn. All research involving human participants must be reviewed no less than once per year. The REC approval for the conduct of a study may be withdrawn if the risks to the research participants are determined to be unreasonably high, for example, more than an expected number of adverse events, unexpected serious adverse events; or evidence that the Investigator is not conducting the study in compliance with national and international guidelines. Such findings may result in a more frequent review of the study to determine if approval should be withdrawn, or enrollment stopped until corrective

measures can be taken, or the study terminated. Continuing review includes, but may not be limited to the following activities:

- Site Visits and Third-Party Verification
- Review of Serious and Unexpected Adverse Events
- Review of Amendments
- Review of Significant New Findings
- Reports from Supervisors (for students), Employees, Staff and Faculty
- Noncompliance

3.4.8.1 Types of follow-ups

The follow-up visits from by the REC are conducted either; **On-site:** This is monitoring performed at the research site. This can only be done physically. **Off-site:** This is the monitoring of studies away from the research site. This can be done virtually or remotely and is where monitors do not visit the site to review the data and related documents but instead, the monitoring is done virtually. With the use of digital technology, this can be done from wherever the monitors are located. Research regulators shall review studies through different data sources including annual progress reports, ethics approvals, monitoring reports, serious adverse events (SAEs) reports, adverse events (AEs), suspected unexpected serious adverse reactions (SUSARs) reports, amendments, and de-identified research participants' documents. Consideration must be made to ensure the privacy and confidentiality of participants.

Case Study

18 November 2012. Company ABC sponsors a Phase III trial on an investigational new drug for the treatment of tuberculosis. Site YZ has already recruited 60% of the patients for the study. Today, the clinical monitor on site for the routine monitoring visit calls the sponsor to seek advice. During the review of the study documents/investigator file, he noted that the renewal of the approval of the local REC was not on file. When he asked the principal investigator (PI), he was told that the new approval had not yet been received. The last approval covered the period from 15/09/2011 to 30/09/2012.

Source: FERCAP/SIDCER Handbook of Case Studies on Ethical Issues in Health Research

Points for Discussion

1. What will your advice be to the monitor?
2. Would you consider any GCP finding under such conditions? If so, formulate your findings.

3. Can the study continue? Discuss new enrolment and follow-up of patients.
4. What corrective action should be taken by the Investigator related to the local REC?

The approval was finally obtained, but after inquiry, it seems that the REC didn't have a lay person and there were no minutes of the meeting.

5. What should the sponsor do, considering that they have more projects that would need to be submitted to this REC?

3.4.8.2 *Continuing Review of Research*

The REC conducts a continuing review of research taking place within its jurisdiction at intervals appropriate to the degree of risk, but not less than once per year.

Interval for Review for Purposes of Renewal: The REC must conduct a continuing review of protocols for purposes of renewal of the REC approval period, at intervals appropriate to the degree of risk, which is determined at the initial review, but not less than once per year. "Not less than once per year" means that the research must be reviewed on or before the first anniversary of the previous REC review date, even though the research activity may not have begun until sometime after REC gave its approval. Investigators are required to submit a periodic report before the expiration of the study or as specified by the REC, but at least annually. The report should normally be filed within 60 days before the study approval period ends.

Extensions of Approval Period: There is no grace period extending the conduct of the research beyond the expiration date of the REC approval. Extensions beyond the expiration date are not granted by the REC. If Continuing Review Report forms and other requested progress reports are not received as scheduled, the Investigator must suspend the study, including study enrollment and data collection until reports are reviewed and approved.

Review of the progress reports: All REC members shall receive a progress report prepared and submitted by the Investigator along with the number of research participants entered to date and since the last review. The progress report shall summarize adverse event experiences, amendments, and new conflict of interest disclosure as applicable, and provide a reassessment of the risk-to-benefit ratio.

3.4.8.3 Self-Evaluation of RECs

The self-evaluation process involves reviewing the committee's policies and procedures, examining how well they are being followed, and seeking feedback from committee members and stakeholders. By conducting a thorough self-evaluation, the committee can ensure that it is operating ethically and effectively and make any necessary changes to improve its performance in reviewing research proposals. Regular self-assessment is essential for maintaining the committee's credibility and integrity in upholding ethical standards in research. The REC should have Standard Operating Procedures (SOPs) for internal reviews, the outcomes of past and present reviews, and documentation of follow-up actions taken by the REC in response to the reviews, including modifications to the ethics review process, in its standard operating procedures and other documents outlining the mechanisms for conducting regular internal reviews of its performance.

The REC should conduct regular internal evaluations of its performance to ensure high standards of quality and productivity, and to protect research participants. For most RECs, the reviews should be conducted annually; however, RECs with a very low volume of work or that review only minimal-risk studies might choose to conduct them less frequently. RECs should select criteria for the review based on applicable legal standards, ethical guidance, and internal policies and procedures. The REC should use the information from these reviews to continually improve the ethics review process. The REC should assess if its staff and members consistently adhere to its policies, rules, and procedures, focusing on consistent application of international guidelines and national standards. This could be achieved through interviews, regular review of meeting minutes, and self-assessments of selected protocol reviews.

The REC should gather feedback from researchers and study participants to enhance ethics oversight. If feedback indicates issues with the research, the REC may suspend or stop the study. If the feedback reveals issues with the ethics review procedure, modifications should be implemented. Researchers and participants should be able to anonymously submit comments through the REC. This will ensure transparency and encourage open communication between all parties involved in the research process. By actively seeking and addressing feedback, the REC can work towards improving the overall ethics oversight of research studies and better protect the rights and well-being

of study participants. Ultimately, this collaborative approach will help to uphold the highest ethical standards in research practices.

The criteria for measuring the effectiveness of the REC include;

1. Measures of productivity, such as time between submission and approval.
2. The quality of REC deliberations, such as reviews of meeting minutes to determine whether all relevant ethical criteria are discussed and whether sufficient attention is paid to core issues such as risk-benefit assessment and informed consent.
3. Comparison of the REC's assessment of the risk of studies with information on the number and types of adverse events reported in those studies.
4. The number and nature of complaints received by the REC.
5. Feedback from REC members about the strengths and weaknesses of the ethics review process.

3.4.9 Exchange of RECs with Other Bodies

Research regulatory bodies and stakeholders collaborate to share best practices and promote harmonization in ethical considerations in research. Oversight authorities ensure compliance with RECs to maintain integrity and safety in human subject research. They protect participant rights, build trust, and ensure responsible conduct of studies, enhancing the overall research process. This approach ensures high standards for all parties involved. By collaborating with other bodies, RECs can also stay up to date on the latest developments in research ethics and adapt their practices accordingly. Ultimately, this communication fosters a sense of transparency and accountability within the research community, promoting trust and integrity in the research process.

Government agencies can enhance the effectiveness of RECs through continuous technical support, coordination, and monitoring. Oversight bodies can support training initiatives, encourage coordination, spread best practices, and facilitate communication among RECs, national regulatory agencies, and other research stakeholders.

The national and international research regulatory entities can conduct REC regular needs assessments to identify activities that would be most helpful and collaborate with them to create and execute rectification programs, while also addressing violations

of legal and ethical norms. Responsibility for overseeing RECs can be vested in independent agencies created for this purpose or in existing government agencies such as ministries of health. Entities with oversight responsibility should be given the legal powers and resources necessary to carry out their mission, including the authority to conduct audits of RECs on a routine or for-cause basis.

The joint review and inspection of research studies by international and national agencies and RECs enhances the capacity to make evidence-based decisions. This collaborative approach allows for a comprehensive understanding of potential risks and benefits of new developments in research and technology, ensuring that decisions are grounded in the most up-to-date evidence. This approach also ensures effective and ethical oversight of research activities, protecting participants and upholding the integrity of the research process. Therefore, the exchange with other bodies enhances the quality of the review of protocols, optimizes review timelines, facilitates the exchange and validation of findings by regulators, sponsors, and RECs, and acts as a capacity-strengthening platform.

3.4.10 Independent Audit of REC Functioning

The independent audit operations of the REC ensure effective support of the REC's mandate. The quality assurance of the REC is essential to ensure that ethical guidelines are being followed and that research participants are being protected. By conducting regular audits, any issues or areas for improvement can be identified and addressed promptly. This helps to maintain the integrity of the research process and uphold the trust of both participants and the broader scientific community. Therefore, the audit consists of three components: Regular review and assessment of standard operating procedures (SOP); Ensuring the REC staff have the required education, experience, and training to perform their duties appropriately and Ongoing assessment of the REC operations and outputs.

3.4.10.1 Internal Audits of the REC Operations

The ongoing assessment of the REC operations and outputs is conducted through Quality Control (QC) monitoring and Quality Assurance (QA) auditing (internal and external). The QC monitoring involves periodic, real-time checks of specific REC operations, documents, and records. The institutions or government bodies perform these QC steps on a routine basis. Internal auditing is a retrospective assessment of the

REC operations through document and record review. Internal audits may be horizontal, where a particular function is assessed across several studies (e.g., minute-taking); or they may be vertical, where a particular study is audited in whole or in part (e.g., high-risk research). An independent auditor performs internal auditing on at least an annual basis.

3.4.10.2 External Audits of the REC Operations

External audits of the REC operations are essential in ensuring that the committee is following all necessary guidelines and regulations. These audits help to identify any potential areas of improvement or non-compliance, allowing the committee to make necessary adjustments to their operations. By conducting external audits regularly, the REC can maintain a high level of integrity and trust within the research community. The external audits are performed by the national regulatory agencies or government bodies to provide an additional assessment of the quality of the REC operations. The regulatory agencies that accredit the RECs have the authority to audit the operations of REC and support such audits as part of its continuing effort to maintain high standards for scientific quality and human research protections.

3.4.11 Communication with Researchers and Sponsors

REC communication with Researchers and Sponsors is of utmost importance in ensuring that all parties involved understand and adhere to ethical guidelines throughout the research process. Clear and open communication allows for any potential ethical concerns or issues to be addressed and resolved in a timely manner. This collaboration between researchers, sponsors, and the REC ultimately helps to protect the rights and well-being of research participants and uphold the integrity of the research study.

Maintaining open and transparent communication with researchers and sponsors throughout the review process, providing feedback, addressing concerns, and ensuring clarity on ethical requirements are crucial to building trust and collaboration between all parties involved, ultimately leading to a more successful and ethical research project. By keeping all stakeholders informed and involved in the decision-making process, potential conflicts and misunderstandings can be avoided. In addition, clear communication helps to uphold the integrity of the research and protects the rights and well-being of the participants involved.

In carrying out effective business, REC must ensure that all the partners and stakeholders follow the best communication practices. Keeping proper communication records is paramount for keeping track of the information flow of correspondence. The REC will have an SOP to ensure proper compilation, distribution, and filing of verbal and written communication and other study-related or process-related information done with the REC members, investigators, sponsors, volunteer participants, institutes, and/or relevant government agencies.

3.4.12 REC Correspondences

Accurate records of all communications to and from the REC shall be maintained. All copies shall be filed in the REC's investigator project file. Hard /soft copies of all correspondence between the REC, sponsors, and the investigators, shall be kept in the investigators' protocol folders. Hard and soft copies of approved documents shall be shared with the sponsors/or the investigators. It is the responsibility of the REC to keep a communication log to track correspondence and information flow between the REC, investigators, and other stakeholders. Items to document shall include among others: The date when the protocol is submitted, the date protocol is assigned to reviewers, assigned lead reviewers, the expected review date, the date feedback is sent to the investigator, the document date of protocol approval, the date letter picked where applicable, communication log, etc.

Case Study

A REC approved the protocol and informed consent form (ICF) for a randomized double-blind clinical trial about the emergency use of an investigational drug vs. placebo in comatose patients. The monitor went to the site for the monitoring visit and called the sponsor because she found that a patient's husband had given consent to enroll his comatose wife. As a sponsor, you checked the REC approval and found out that the REC only approved a patient consent form. There was no consent form for a legally acceptable representative.

Source: FERCAP/SIDCER Handbook of Case Studies on Ethical Issues in Health Research

Questions for Discussion

1. What should the sponsor (project manager) do next?
2. What did REC miss when it reviewed the protocol?
3. Identify the REC deficiencies and what corrective action should be done?
4. Identify the REC SOP issues

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4 Module 4: A Guide for the Ethical Review of Research Proposals for RECs

SCOPE OF THE MODULE

This training module provides a comprehensive overview of the ethical review process for research proposals, guiding researchers through the practical steps required to maintain ethical standards and protect the research participants. It provides essential information on the proposal review processing activities involving application procedures, conflict of interest management, documents required for submission, research participants recruitment information, risk assessment and management methods, and informed consenting procedures. This module is essential for Research Ethics Committee (REC) members and researchers to better understand the research proposal requirements to be submitted for review and to create insight into safeguarding the rights of research participants, promoting transparency, and ensuring research accountability.

LEARNING OBJECTIVES

Upon completing this module, the training participants will be able to:

- Understand and effectively manage the application process for ethical review,
- Identify the required documents and procedures for submitting proposals for ethics review.
- Recognize and manage potential conflicts of interest in research ethics
- Identify essential components of ethical procedures for safeguarding vulnerable study participants
- Understand the benefits of study participation and ensure ethical considerations.

4.1 Definition

Research Proposal Application Process for Ethics Review refers to the formal and systematic procedure by which researchers submit their planned study protocols to a REC for ethical evaluation. The purpose of this process is to evaluate whether the proposed research meets established ethical standards, protects the rights, safety, and well-being of participants, and complies with the relevant institutional, national, and international guidelines and regulations. This process typically includes the submission of detailed information about the research design, objectives, methods, informed consent procedures, risk-benefit analysis, and data management plans including relevant required documents. Approval from the ethics review body is required before the research begins, ensuring that the study is ethically sound, responsibly conducted and will not harm study participants.

4.2 Research Proposal Application Process for Ethics Review

Understanding the Standard Operating Procedures (SOP) of the ethical review process helps researchers to prepare and submit proposals to the REC as per the requirements. This process is guided by the SOP of the designated institutional REC. REC often adapt their working SOP from the national and international guidelines. The SOP contains the steps for submitting proposals, required procedures and documents, and timeline for the review process. The guideline brings researchers and REC on the same page and ensure all necessary materials are complete and well-organized for a smooth review. This process is vital to handling conflicts of interest among REC members and complaints that could arise from researchers and study participants. Any REC member with a conflict of interest must be excluded from the proposal review process to avoid making biased decisions. Likewise, researchers submitting the research proposal for ethical review should not have a conflict of interest, transparent and free of bias. The SOP is vital to guide both researchers and REC to make the right decision and protect the vulnerability of the study participants.

The WHO standards and operational guidance for ethics review of health-related research with human participants urges that the REC's policies and procedures should describe the requirements for submitting an application for review, including the forms to be completed and the documents to be submitted. This guideline further elaborates the need for specifying the process and procedure for review, the process for coordinating review with other committees, the process for setting up meetings, circulating documentation for the meetings, inviting non-members of the REC, approving the meeting minutes, and any related process issues. Procedures for deliberation and decision-making are clearly established and described based on the established standard operating procedures including the maximum amounts of time between submission and decision. The following group exercise and reading materials provides you with better understanding on this topic.

Activity 4.2: Discuss in group and reflect your experiences

Questions for discussion

1. What research ethics review operational guidelines do you know?
2. What are the similarities and differences between your SOP and those International SOPs?
3. What are the gaps?
4. What were the main challenges you faced in using your SOP?

4.3 Information Required for REC Proposal Review

4.3.1 Description of the project

A research proposal to be submitted for ethical review requires a detailed description of the research project. This section breaks down each component of the research proposal necessary for the submission requirements to ensure its clarity and transparency. Training participants will learn the specific requirements of the research proposal to be submitted for ethical review. The proposal should make a detailed description of the researcher qualifications, funding sources, project objectives, and scientific justification, demonstrating how the study contributes to existing knowledge. The proposal also contains a detailed research methods and procedures, covering sampling, statistical techniques, and analyses to ensure scientific rigor. Additionally, a plain-language summary is required to help non-experts REC members understand the research objectives. Information on the study population, recruitment processes, data confidentiality, risk management, and potential benefits must be included to inform the RECs for their comprehensive assessments. Furthermore, the research proposal should contain a detail budgeting, funding transparency, and data handling and management procedures to ensure financial and operational feasibility of the project within the given contexts. The implementation competence of the research with the supporting documents like curriculum vitae and other members professional competence should be included in the proposal as annex to ensure that the proposed research project achieves its objectives. The following case study (Case Study 1) will provide the training participants the importance of submitting the research proposal with all the necessary requirements to ensure an unbiased decision.

Activity 4.3.1: Read the following case study, discuss in group and present in class.

Case Study: Scientific Soundness

A newly formed company prepared a protocol with the objective of proving the health benefits of water processed by an imported machine to HIV positive patients. They chose a sanitary engineer as PI and submitted the protocol to the hospital REC. Since the investigational product was water, the REC approved the protocol and informed consent form (ICF) immediately.

Source: FERCAP/SIDCER (2012), Handbook of case studies on ethical issues in health research, page 11

Questions for discussion

1. What is the General Clinical Practice (GCP) issues related to the case study?
2. What is the role of sponsor, role of investigator, and role of IRB?
3. Was the hasty approval justified?
4. What information should the REC require in the protocol? In the ICF?
5. What kind of investigator expertise does the protocol require?

4.3.2 Recruitment and Selection of Participants

The research proposal must provide sufficient information to ensure fair and equitable selection of the study participants by avoiding recruitment biases and ensuring a diverse and representative sample. This helps to reduce potential vulnerabilities of the specific groups and evaluating procedures to avoid coercion or exploitation during recruitment. This section provides information on ethical recruitment strategies that ensure fairness and representativeness in participant selection. Training participants will learn the importance of creating a recruitment process that is inclusive and unbiased, focusing on obtaining a diverse and representative sample. Vulnerable groups, such as economically disadvantaged individuals or those with limited autonomy, are not coerced into participation and the recruitment processes followed transparent methods.

4.3.3 Risks and Benefits of the Research

Minimizing harm and vulnerability of the research participants is a core ethical principle. This section of the research proposal covers methods for evaluating the risk-benefit ratio of the proposed research. Training participants will learn how to assess potential risks and benefits, by considering the probability of harm, safety measures, and participant well-being. This section highlights the importance of balancing risks and benefits for individual participating to the study as well as their community. Hence, training participants will learn and develop the skills to critically analyse the submitted proposal for review and assess and balance risks and benefits without breaching ethical principles. This section additionally considers strategies for benefit sharing as a post-trial access (PTA) to the study participants as well as their community.

Activity 4.3.3: Read the following case study, discuss in group and present in a class. During your discussion emphasize on the sufficiency of the information on the benefits and potential risks.

Case study: Grace's Clinical Trial Experience and related ethical breach

Grace is a 24-year-old Zimbabwean woman diagnosed with HIV in 2005, was enrolled in the EARNEST clinical trial in 2010 after her first-line treatment has been failed. The trial, funded by European agencies and pharmaceutical companies, aimed to test second-line antiretroviral therapies in resource-limited settings. Grace was randomly assigned to a treatment regimen that included Aluvia (Lopinavir/Ritonavir) and Raltegravir, later switching to a boosted protease inhibitor monotherapy.

Shortly after starting the trial, she developed severe vision problems, which were not disclosed as a possible side effect in the informed consent process. Despite multiple attempts to get help from EARNEST, she was only referred to an optometrist who confirmed irreversible eye damage upon complaining her case. As her condition worsened, Grace faced social and financial struggles, including

abandonment by the father of her child. She later discontinued the trial drugs due to suspected harm but struggled to return to her previous treatment. Grace, finally passed away in April 2014 after her health was deteriorated. Finally, efforts to seek legal redress by the investigative Journalist who contacted her failed due to missing documentation, including the signed informed consent form. Her child had also died because of lack of care by her family.

Source: Adapted from Wemos (2015). Clinical trials realities in Zimbabwe: dealing with possible unethical research, page 15 – 20. <https://www.wemos.org/wp-content/uploads/2023/04/Clinical-Trials-Realities-in-Zimbabwe.pdf>

Discussion points

1. Ethical failures in clinical trials involving poor participant selection, lack of transparency, and inadequate informed consent.
2. Side effect mismanagement due to lack of prior warnings about vision impairment and failure to address severe adverse effects.
3. Neglect by EARNEST involving delayed responses, inadequate medical support, and refusal to assist in treatment transitions.
4. Social and economic impact related to disability-related stigma, abandonment, and financial struggles.
5. Barriers to legal support because of missing consent forms and weak participant protections in international clinical trials.

4.3.4 Informed Consent

Informed consent is one of the means of ensuring confidentiality and autonomy of the study participants. Informed consent in research refers to the ethical principle and legal requirement whereby participants voluntarily agree to participate in a study after being fully informed about all aspects of the proposed research. The CIOMS International Ethical Guidelines define informed consent as "consent given by a competent individual who has received the necessary information, has adequately understood it, and has decided without being subjected to coercion, undue influence, inducement, or intimidation." It is a fundamental aspect of ethical research practice and ensures that participants understand the purpose, procedures, potential risks and benefits, and their rights regarding their involvement in the research.

Participation details must be included in the research proposal including the research procedures, potential risks and benefits, the duration of involvement, and any alternatives to participation. It is also crucial to highlight the voluntary nature of participation, reassuring participants that they can withdraw from the study at any time without any pre-conditions. The researchers should clearly outline confidentiality protections, explaining how personal data will be anonymized, stored, and accessed,

and specifying who will have access to the data. Contact information for the researchers and the REC must be included to provide participants with the possibility to ask questions or report any concerns. The study participants must be informed about the use of tissue samples and data for future research and consent for secondary use in the study involves human body samples. This section also provides information on the strategies for obtaining consent from vulnerable population without coercion, providing adequate time for decision-making, and ensuring consent procedures are conducted by qualified personnel. This comprehensive approach helps participants implement ethical consent practices in diverse research settings. Research proposals submitted for ethical review should include detailed information about informed consent, helping the REC make an unbiased decision regarding the approval of the proposal. The discussion of the following case study (Case Study 3) will enhance your understanding of the importance of information in informed consent and its processes.

A study to determine the value of postoperative radiotherapy

Over an 11-year period, a well-respected cancer hospital in East Asia studied a much-debated issue: whether the survival of patients with oesophageal cancer is improved by radiotherapy after resection (surgical removal of the cancer cells). The study did not receive an ethics review before it was started because at the time few research institutions in the country had RECs.

Patients at the hospital who underwent radical resection during this period were randomly assigned into two groups: those who only had surgery and those who also received radiotherapy (treatment with radiation to kill any remaining cancer cells), beginning 3-4 weeks after their surgery. Clinicians told patients in the radiotherapy group that they were being given “innovative therapy”. The clinicians provided complete descriptions of the probable risks and benefits of the treatment, after which patients had the opportunity to accept or refuse it.

None of the patients were told that they were participants in an experiment. The investigators believed that the population under study had such a strong, culturally rooted distrust of medical science that even simply using the term “research” would trigger a refusal by most patients to participate. The investigators reasoned that since the patients received all the information relevant to whichever intervention they were being offered and were free to accept or refuse that treatment, their oral approval was sufficient to keep the study in compliance with prevailing guidelines for informed consent.

The researchers submitted their results, which lent substantial support for postoperative radiotherapy in the treatment of oesophageal carcinoma, to a well-respected medical journal in the North America. After some deliberation, the journal’s editor decided to print the paper but invited an editorial from a North American physician and ethicist who criticized the lack of informed consent and ethical review, adding that violations of human rights were frequent in the country where the study was done. The authors were not shown the editorial nor invited to reply.

Source: WHO (2009), Casebook on ethical issues in international health research, page 97

Questions for discussion

1. Do you agree with the investigators' ethical justification of their decision not to tell patients that they were in an experiment? Why or why not?
2. What harm, if any, did the patients experience because they were not informed that they were participants in a study?
3. Though now widely introduced, formal mechanisms for informed consent and prior ethical review were not standard in the country when the study was done. Is it appropriate to use today's ethical standards to judge a study that began years ago?
4. Should the journal have printed a study that reviewers found unethical? When, if ever, is the scientific value of a study significant enough to justify publication despite ethical violations?
5. Should the authors have been given the opportunity to reply to the editorial?
6. Did the journal editor adopt an ethical approach by publishing an editorial against a published study without informing the investigators?

4.3.5 Additional information for the application processes

4.3.5.1 Confidentiality of the participants

The confidentiality of the study participants must be maintained by implementing robust data security and privacy measures including sensitive information. This could include encryption of digital files, security of physical storage for hard copies, and restricted access to personal identifiable data. Participants should be reassured that their identity will not be disclosed in research reports or publications and any shared data will be anonymized to prevent reidentification. Moreover, transparent communication should be made with the study participants during informed consenting about the data-sharing agreements and plans for data destruction after completion of the study. Moreover, the informed consent should also ensure participants about their safety and establish clear procedures of proactively identifying and mitigating potential risks. Safety measures must include ensuring that the research environment is secure, free of hazards, and supportive for participants. Most importantly, the prevailing cultural contexts of the study participants and their status must be given due consideration and maintained.

Activity 4.3.5A: Read the following case study on privacy and confidentiality of the participants, discuss in group and present in a class.

Case Study: Qualitative research of unplanned teenage pregnancy

Unplanned pregnancies are pregnancies that are mistimed, unplanned or unwanted at the time of conception. It is related to numerous maternal and child health problems especially in pregnant teenagers. This situation sometimes forces them to seek abortion which often causes serious complications, particularly in cases of septic abortion.

An experienced social scientist who works at a family planning clinic at a provincial hospital submitted a protocol to the REC for review and approval. The investigator proposed to investigate the attitudes of unplanned pregnant teenagers regarding induced abortion. Data from at least ten pregnant teenagers aged between 10-19 years old will be collected using focus group discussion. The investigator plans to approach the participants at antenatal clinic before seeing doctors. If the pregnant teenagers agree to participate, a focus group will be conducted for approximately 60 minutes in that afternoon. The questions used in the focus group will include:

1. What do you think about your unplanned pregnancy?
2. Has getting pregnant damaged your lifestyle? How?
3. Have you ever heard about unsafe abortion? If yes, what do you think about this?
4. Have you ever heard about the risk or consequences of unsafe abortion? How?
5. What do you plan to do with your life after this?

During the discussion, the investigator plans to record the conversation by video recorder to ensure the correctness of the data.

Source: SIDCER (2019), A Casebook for Reflecting on Challenges and Aspirations for Improving the Role and Function of Ethics Committees and Ethical Review Systems, page 19

Questions for discussion

1. Is the data collection method appropriate?
2. Is the principal investigator qualified to conduct this study?
3. Do the participants have direct benefit? What about possible risk?
4. Is informed consent necessary? Why?
5. Should the informed consent from the parents be obtained?

4.3.5.2 *Conflicts of Interest*

Financial interests that may influence the conduct of the research or the interpretation of its results must be disclosed, and mitigation strategies should be developed. Conflicts of interest can involve both financial and non-financial interests. Financial interests may include funding from sponsors or personal investments related to the research outcomes, which can introduce bias. Researchers must disclose any such conflicts to the REC and participants and implement safeguarding approaches, such as blinded analyses, to ensure unbiased results. Non-financial conflicts may arise from

personal relationships, academic competition, or institutional pressures. Procedures for managing these conflicts must be clearly outlined in the proposal and communicated to REC effectively.

4.3.5.3 *Financial compensation*

Compensation for participation in the research should be fair, proportionate, and not so high to constitute undue inducement during participation. Assessing the appropriateness of compensation through reviewing of payment structures and its reasonability must be ensured and clearly indicated in the proposal. The compensation should reflect the time, effort, and potential inconvenience or risks to participants without exerting undue influence. All financial aspects of the research, including compensation structures and funding sources, must be clearly communicated to participants as transparency builds trust and ensures informed participation. This information should be clearly presented in the proposal and effectively communicated to REC to eliminate any potential influences and conflicts of interest.

4.3.5.4 *Financial compensation for Vulnerable Populations*

Identifying and protecting vulnerable populations is very crucial to maintain ethical conduct of research. Recognizing specific populations that may require additional protections, such as children, prisoners, pregnant women, individuals with cognitive impairments, or those from marginalized communities. Training participants will learn about culturally sensitive consent processes, the importance of legal representatives, and modifications in the consent process that are necessary to protect the rights and welfare of vulnerable participants. Special considerations for these groups reflect the ethical obligation of the researchers to respect and protect populations that may be at a higher risk for exploitation or harm. Researchers must include strategic approaches that can safeguard against the potential exploitability of these populations during their participation in the study.

Activity 4.3.5B: Read the following case study on vulnerability of the participants, discuss in group and present in a class.

Case study: Pharmacokinetic and pharmacodynamics studies of efficacy, tolerability and safety of higher dosage Rifapentine for treatment of TB.

Edwin is a 47-year-old man from Manyatta estate, Kisumu, Kenya, who unknowingly participated in a clinical trial for higher doses of Rifapentine, a TB treatment drug. Living in extreme poverty, he repaired and resold plastic items, which barely allowed him to afford basic needs. In 2012, after feeling ill and experiencing symptoms of coughing up blood, Edwin sought medical help using his mother's savings. He

was subsequently diagnosed with TB and approached by researchers from the CDC/KEMRI at the local hospital, who offered him free treatment as part of the study.

Although Edwin signed a consent form in his native Luo language in the presence of a doctor, he was unaware that his treatment was part of a clinical trial. The trial aimed to test the efficacy, tolerability, and safety of higher doses of Rifapentine in curing TB more quickly. As part of the trial, Edwin received medication, daily food parcels, and transport money for six months. However, he later developed adverse effects, including excessive sweating, joint pain, and worsening eyesight, which affected his ability to work.

Despite the consent form stating that participants would receive medical care for any trial-related issues, Edwin received no follow-up visits. He believes his eyesight problems are linked to the medication but feels powerless to seek help. He was also asked to work as a tracer to find other TB patients but refused due to the lack of post-trial support. Detail of this case is available in the link below.

Source: Adapted from Wemos (2017), Clinical trials In Africa the cases of Egypt, Kenya, Zimbabwe And South Africa, page 13 - 17 https://www.wemos.org/wp-content/uploads/2023/04/Clinical-trials-in-Africa_2017.pdf

Discussion Points

1. Poverty and limited access to healthcare services: Edwin's financial struggles forced him to seek free treatment, leaving him with no real choice.
2. Ethical concerns in informed consent: He unknowingly participated in a clinical trial without fully understanding its implications.
3. Trial experience and social stigma: up on receiving food and transport money, he faced social stigma and misunderstandings about his condition.
4. Post-trial health complications and neglect: he developed serious side effects, including worsening eyesight, but received no medical follow-up.
5. Broader ethical implications: concerns over informed consent, post-trial care, and the exploitation of vulnerable populations in clinical research.

4.3.5.5 Community Engagement

Finally, this module addresses the importance of scientific merit, validity and rigor to ensure that the research proposals have a strong, evidence-based rationale and is likely produce reliable and meaningful results. Additionally, the research must explore the role of community engagement in fostering trust, honouring local values, and ensuring respectful collaboration. Involving the community in the research from the beginning can help researchers address concerns, prioritize community problems, and enhance the ethical and societal impacts of their research.

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5 Module 5: Specific Ethical Issues in Research

SCOPE OF THE MODULE

This module provides a detailed understanding of ethical concerns that guide the research processes in transnational research, adaptive trial designs and decentralized studies ensuring the integrity of the research and the well-being of participants in these research studies. Issues to be covered include safeguarding and use of human biological materials, data collection, storage, and use, the use of placebos, modifications and waivers of informed consent, and decentralized and adaptive clinical trials. This module equips learners with the necessary skills to understand and apply ethical guidelines governing research processes.

LEARNING OBJECTIVES

Upon completion of this module, participants will be able to:

- Describe the ethical principles that guide the conduct of transnational research.
- Understand the ethical principles of obtaining informed consent in transnational research.
- Understand the ethical concepts related to protecting the rights of research participants.
- Understand ethical considerations in data collection, storage, and usage.
- Understand the ethical principles of using placebos.

5.1 Transnational research, Adaptive trial designs and Decentralized studies

5.1.1 Definitions

Transnational research crosses national borders, involving cross border collaborations between researchers from different countries who work together to share knowledge and resources, often with the goal of addressing global challenges (Ward 2021). It could also be collaborations between partners to provide a network structure that uses multiple methods and technologies to harmonize parameters such as complexity, expertise, safety, and efficiency with national regulations, institutional policies, and best practices. There is an increase in transnational research, especially with the increase in outbreaks and pandemics. Adaptive trial designs are studies that use the cumulative results from the study to modify the trial design following the trial predetermined rules, while decentralized studies involve some or all the research activities occurring at locations other than a traditional research site aimed at reducing the need for physical visits.

5.1.2 Ethical Concerns in these designs

While these designs benefit from new tools such as artificial intelligence and big data analysis platforms, they also face ethical and legal complexities. Researchers must be aware of these ethical concerns, follow international guidance in the design and conduct of these studies.

5.1.2.1 *Transnational Studies*

In addition to the standard ethical concerns for research involving human participants, transnational studies have several ethical challenges and concerns including inequalities in national and institutional capacity to conduct health research which can influence how low-resource countries benefit from the research. These disparities also affect the ability of RECs, the lengths and bureaucracies of the review and approval systems, and cultural differences. Transnational requires careful consideration of ethical guidelines and regulations in different countries such as low-resource settings which present unique ethical challenges. These challenges arise from factors such as poverty, limited healthcare access, and cultural differences. Transnational research involving participants from low research settings must ensure that participants are recruited fairly and without exploitation, ensure that participants are not coerced into participating in the research. It is important for researchers to respect local customs and norms related to privacy and confidentiality, ensure fairness in collaboration. Promote knowledge transfer and support sustainable research infrastructure. Capacity building in Low- and Middle-Income Countries is crucial for strengthening research capabilities and fostering sustainable collaborations with high-income countries. By strengthening capacity building, we can enhance the quality of research, address local health challenges, and contribute to global health knowledge. Develop strategies to ensure that benefits, such as new treatments or technologies, are equitably distributed among the population.

5.1.2.2 *Adaptive Trial Designs*

While Adaptive Clinical Trials (ACTs) are increasing in prominence, they pose ethical issues that should be considered in the design, conduct, analysis and reporting of the trials (Singh 2023). According to the WHO guidance on ethics for ACTs, there are 9 ethical challenges that need to be considered while designing, reviewing and conducting ACTs.

- a. *Delays in the ethical review process*: Just like the transnational research studies, convoluted ethical review processes are a challenge to ACTs, and efforts must be made to reduce this time. Initiatives such as joint review of protocols and project management approaches that eliminate low priority activities should be adopted.
- b. *Social value and inclusion*: The social value of ACTs is that they provide innovations/ interventions to the public that may not be provided by conventional trial designs. This is more important during epidemics and outbreaks where conventional trial designs may not be appropriate. However, who participates in the study and how they are chosen to participate is a big challenge to ensure inclusivity and benefit from the innovations. If groups such as pregnant women and children are not included in the trials, then they cannot benefit from the innovations of the trial. Similarly, if some regions or countries are not included, then they may miss out on the benefit of the findings of the study. Additionally, which stakeholder's ideas gets included in the adaptive design also comes to the fore in such circumstances. As not all interventions will be available or feasible in all settings, the choice of interventions to be included in a multi-country platform trial has ethical implications for future access.
- c. *Stakeholder engagement*: It is important to have effective stakeholder engagement during the design of the trial to ensure that the design is informed by as many stakeholders as possible. The degree of influence of stakeholders that is genuinely possible at different stages and under prevailing time pressures needs to be well described. There should be some flexibility to adapt certain aspects of study conduct to make them locally appropriate and sensitive. Most existing guidance on engagement was developed for conventional trials, ACTs which are based on networks and creation of platforms across multiple countries, pose new challenges. There is a need to carefully develop a strategy to achieve genuinely respectful engagement, allowing for a voice in both the choice of priorities for design and the way in which the research will be conducted.
- d. *Equity and sustainability in partnerships* ACTs have mainly been implemented in the developed countries and thus bear the risk of low generalizability in the low-income countries. However, these trial designs are gradually being implemented as collaborations between the northern and southern partners. This raises the issue of equitable partnerships which need to be promoted at institutional level through initiatives such as the Research Fairness Initiative (<https://rfi.cohred.org/>). This includes the way studies are conducted at different

sites, the roles of the various stakeholders and the terms of how the focus of research is decided.

- e. *Governance* ACTs raise questions for internal governance mechanisms. This is particularly challenging during outbreaks and epidemics. Key concerns to consider include:
 - How can values be built into governance mechanisms?
 - What is the place of governance arrangements in each platform trial? Specifically, how is accountability balanced between the “coordinating center” and individual sites or countries?
 - Who determines what goes into key documents such as partnership agreements, the terms of reference of the different governance structures of the trial team or material transfer agreements?
 - And what scope is there for new partners to exercise any influence, as new sites are added to a trial that is already well established?
- f. *Tension between universality and pluralism in platform trials*: ACTs are conducted based on centrally developed protocol which requires some degree of adherence to its processes and methods. This requirement for universality and the ethical imperative of conducting the study in a manner that is sensitive to the local context raises a challenge that needs to be addressed. While maintaining consistency to the core aspects of the protocol is essential, there is need for sensitivity and adaptation of other aspects of the study such as appropriately designed recruitment procedures for different sites. Other factors that may impact local acceptability include which the arms of the study respond to local needs and the role of local stakeholders in governance arrangements.
- g. *Informed consent* is one of the key challenges in ACTs that require attention. The complexity of ACTs (design and conduct) raises specific challenges for informed consent processes, especially how best to share information about the features of the trial in ways that help people to make decisions. Participants’ information documents in conventional trial designs clearly describe the interventions and potential arms to which the participants will be randomized. However, in ACTs, participants may change the intervention arms during the study, and this needs to be highlighted and explained to the participants in a language they understand.
- h. *Technical issues* like scientific equipoise, fair treatment of participants, and access to effective interventions for study participants are the other ethical issues to be considered. ACTs are liable to the risk of losing the scientific

equipoise that underpinned the trial, and care must be taken in the design and conduct of the trial to ensure that equipoise is maintained

- i. Other areas of concern include capacity building and technology transfer for the less developed partners. In addition, therapeutic misconception also needs to be addressed.

Case Study: ANTICOV – Adaptive Platform Trial for COVID-19 in Sub-Saharan Africa

The **ANTICOV** trial is a large-scale, multi-country **adaptive platform trial** initiated to identify effective treatments for mild to moderate COVID-19 cases in sub-Saharan Africa. Launched across 13 countries—including Burkina Faso, Cameroon, Côte d'Ivoire, the Democratic Republic of Congo, Ethiopia, Ghana, Guinea, Kenya, Mali, Mozambique, Sudan, and Uganda—the study aims to evaluate the safety and efficacy of various treatment regimens in real-world, resource-limited settings.

Adaptive Design: The trial employs an adaptive platform design, allowing for the addition or removal of treatment arms based on interim analyses. This flexibility enables the study to respond dynamically to emerging data and evolving pandemic conditions.

Collaborative Network: ANTICOV brings together a consortium of African and international research institutions, fostering capacity building and knowledge sharing across the continent.

Focus on Accessibility: By targeting mild to moderate cases, the trial seeks to identify treatments that can prevent disease progression, thereby reducing hospitalizations and easing the burden on healthcare systems.

Ethical Considerations: The adaptive nature of the trial introduces several ethical challenges, including ensuring informed consent amidst changing protocols, maintaining equitable access to interventions, and upholding data integrity across diverse settings.

Reference: European & Developing Countries Clinical Trials Partnership (EDCTP). (2020). [Largest clinical trial in Africa to treat mild to moderate COVID-19 patients launched in 13 countries](#). EDCTP

Discussion Questions for REC Members

1. **Informed Consent:** How can researchers ensure that participants are adequately informed about the adaptive nature of the trial, including potential changes in treatment arms or study protocols?
2. **Equity and Access:** What measures should be implemented to guarantee equitable access to trial participation and interventions across different communities and countries involved in the study?
3. **Data Integrity:** How can the trial maintain data consistency and integrity across multiple sites with varying levels of resources and infrastructure?
4. **Regulatory Oversight:** What role should local and international regulatory bodies play in overseeing adaptive trials to ensure ethical standards are upheld throughout the study's duration?
5. **Community Engagement:** How can researchers effectively engage with local communities to build trust and ensure cultural sensitivities are respected in the trial's design and implementation?

5.1.2.3 Decentralized Clinical Trials

Decentralized studies minimize or eliminate the physical access of trial facilities by study participants. These study strategies depend on approaches such as e-consent, wearing of devices and telemedicine among others. They involve taking the study site to the participants' home such as drug delivery or using a community health setting as a study site. How RECs evaluate these studies is critical and adequate assessment tools and a suitable regulatory framework are needed for these reviews.

Some of the ethical issues to be considered include:

- a. *Informed consent* Since most DCTs use e-consenting, care needs to be taken to ensure completeness and clarity of the information provided to the participants. There must be mechanisms for verifying and guaranteeing the electronic signatures provided by the participants. There should be provisions for face-to-face meetings in case the participants need to interact with the investigator.
- b. *Access* The need for advanced technologies may exclude many individuals from participating in the study. This should be minimized either through provision of the technology and/or training that is needed by participants and their caretakers on the use of the different technologies.
- c. *Data collection and transmission* Several considerations need to be made in the data collection and transmission. The methods of data collection should be:
 - lawful and fair and transparent.
 - Accurate and updated
 - Data processing and storage must be restricted
 - There must be adequate minimization of personal data
 - There should be guaranteed confidentiality and integrity
- d. *Protocol Flexibility* There may be variations in patients' preferences, with some preferring direct personal contact while others want the virtual strategy. Participants should therefore be encouraged to provide constant feedback about their preferences.

- e. *Return of results* Special considerations must be taken to ensure that participants receive the results from the investigations and procedures they undertake.

Case Study: Decentralized Malaria Clinical Trial in Mozambique and Kenya

Overview

A decentralized clinical trial was conducted in Mozambique and Kenya to evaluate a novel malaria intervention. This trial employed a decentralized approach, integrating mobile health technologies and remote data collection methods to facilitate participation across diverse and often remote populations.

Key Features

Decentralized Design: The trial utilized mobile health (mHealth) tools to collect data remotely, reducing the need for participants to travel to centralized clinical sites.

Community Engagement: Local community health workers were trained to assist with data collection and participant follow-up, ensuring cultural sensitivity and improving participant retention.

Technology Integration: The study incorporated electronic data capture systems and telemedicine consultations to monitor participant health and manage adverse events in real-time.

Challenges Encountered

Infrastructure Limitations: Inconsistent internet connectivity and limited access to electricity in certain regions posed challenges for real-time data transmission and device charging.

Regulatory Hurdles: Navigating the ethical and regulatory frameworks across two countries required extensive coordination and adaptation of protocols to meet local requirements.

Training Needs: Ensuring that all staff and participants were proficient in using new technologies necessitated comprehensive training programs and ongoing support.

Reference: *Clinical Trial Vanguard*. (2023). [Unlocking Clinical Trials in Africa: New Insights](#)

Discussion Questions for REC Members

1. **Informed Consent:** How can informed consent processes be adapted to ensure comprehension and voluntariness when conducted remotely or through digital platforms?
2. **Data Privacy and Security:** What measures should be implemented to protect participant data collected and transmitted through mobile devices and electronic systems?
3. **Equity and Access:** How can decentralized trials ensure equitable access for participants in regions with limited technological infrastructure or digital literacy?
4. **Community Engagement:** What strategies can be employed to maintain trust and engagement with communities when traditional face-to-face interactions are reduced?
5. **Regulatory Compliance:** How can researchers navigate varying regulatory requirements across different countries when implementing decentralized trial components?

5.2 Biological Materials of Human Origin

Human biological materials (HBMs) are biological samples, such as blood, DNA, organs, and tissues, obtained from individuals through procedures like surgeries or voluntary donations. HBMs have been instrumental in diagnosing and treating diseases like cancer, heart disease, diabetes, and stroke. Researchers' ability to access blood and tissue repositories has enabled comparisons across disease stages. The collection, storage and use of these biological materials are governed by stringent legal frameworks. These frameworks vary by country, but common legal principles apply globally, and they are important to provide adequate oversight for the research use of HBMs.

5.2.1 Biological materials and ethics considerations:

The collection, storage, and use of HBMs for research purposes present a multifaceted ethical consideration. These ethical considerations are important to ensure that the participants' rights, interests, privacy, and dignity are protected, as well as the integrity of scientific research. The health and well-being of participants should be the first consideration.

Informed consent: There are different things to consider when carrying out research that involves the use of human biological materials. Informed consent must be obtained from individuals participating in the research study. Participants should be provided with clear and understandable information about the purpose of the research, the potential risks and benefits, and how their biological materials will be used and stored. Consent should specify the intended use of the HBMs and if intended to be used for future research. Participation should be voluntary, and participants must freely choose to donate their biological materials without coercion or undue influence. Participants should have the right to withdraw their consent and their biological materials at any time without consequences.

Privacy and confidentiality: Measures should be taken to safeguard participants' privacy and protect their personal information. When possible, HBMs and related data should be anonymized or de-identified to minimize the risk of identifying the participants. HBMs should be stored under appropriate conditions to maintain their integrity. Robust security measures must be in place to prevent unauthorized access, accidental loss and use of participants' data. Rigorous quality control measures should

be implemented to ensure the accuracy and reliability of data. Clear guidelines should be in place for the safe and ethical disposal of biological materials.

Potential harm and risk: The participants should be informed about the potential risk of harm posed by the research, including physical risk resulting from the procedure for collecting the HBMs. Psychological and social risk may occur, for instances where the research findings may have psychological or social consequences for the research participants or their communities, or cause stigmatization or discrimination against certain groups.

Documenting the health conditions of an indigenous community

The farmers and forest workers of a largely rural district of South America have recently renewed contacts with an isolated indigenous community in order to gain access to their natural resources. The public health agency fears that this interaction will cause higher incidences of infectious diseases and possibly mortality in the indigenous people. The agency, therefore, invites a university research team to conduct an exploratory study to document the health conditions of this indigenous community. Financial resources are made available but are conditional upon all expenditures being committed by the end of the financial year – that is within a period of 3 months. The research team accepts the challenge and develops a research study based on both a demographic survey (of every fifth household) and a clinical examination of research participants that includes taking blood samples for haematological, biochemical, and immunological tests. In addition, the investigators consider this a timely opportunity to undertake genetic characterization of this population, and include an analysis for genetic markers. As the community lacks residential addresses, the investigators propose to establish a photographic database to facilitate follow-up with individual participants. After reviewing the protocol, the research ethics committee notes two major concerns: first, the researchers have not provided an adequate justification for blood sampling and, second, safeguards to protect participant confidentiality are lacking. The investigators acknowledge the concerns of the research ethics committee, and promise to contact the public health agency to indicate a possible delay in starting the research. At the same time, however, the investigators feel themselves to be under pressure due to a tight timetable within the university, local preliminary plans, transportation arrangements, mobilization of the study team, and not least, their great motivation for the project. They reason that ethics approval was required only for blood collection and not for the collection of the demographic data. They decide to postpone the clinical examinations and blood collection until the protocol is revised and approved, but, meanwhile, to visit the community and move ahead with the survey research and photographic database. In fact, the investigators view this as an opportune time to begin to build trusting relationships within the community, and therefore to facilitate the consent for blood sampling once the approval of the committee has been gained. Three days after beginning the survey, a 5 year-old child from one of the households selected for the survey comes down with meningitis. Members of the community blame the investigators, claiming that the photographs were being used by the local farmers to harm the tribe with witchcraft.

Source: WHO Casebook on Ethical Issues in International Research

Discussion Questions:

1. Were the investigators correct in their assumption that ethics approval is not required for the collection of demographic profiles? Why or why not?
2. Was what the researchers did “scientific misconduct”?
3. What are the special ethical concerns when dealing with minority or ethnically isolated communities? What safeguards might the ethics committee be referring to?
4. How might collection of blood samples for genetic characterization be harmful to this population?
5. What procedures can be put in place to ensure that this research brings benefit to this population?
6. How could the incident relating to the 5 year-old child have been averted? What, if any, are the investigators’ obligations towards any child who becomes ill during the course of the study?

5.3 Data Collection, Storage, and Use

Some common data collection methods include surveys, interviews, observations, focus groups, experiments, and secondary data analysis. When dealing with data, especially large datasets or data with sensitive personal information, ethical considerations are paramount.

Data Collection: During data collection, the research participants should be fully informed about the kind of data to be collected, and how it will be used, who will have access to the data, and the potential risks involved. All this information be clearly stated, so that individuals or participants should have a clear choice to opt in or out of the research. It is important to collect data that is necessary for the specified purpose of the research, avoid or minimize collecting excessive or irrelevant information. Researchers should be transparent about the data collection practices and ensure that the data collection methods are fair and unbiased.

Data Storage: Protect the privacy of individuals by anonymizing data whenever possible. Ensure that data cannot be easily linked back to individuals without their consent. data privacy, security, and the use of digital technologies. Some best practices for protecting the confidentiality and anonymity of research data includes, instead of using direct identifiers like names or social security numbers, assign unique codes or pseudonyms to participants; store identifying information separately from the research data. This creates a barrier between the data and the participants' identities. Remove or mask any identifiers before sharing data for analysis or publication. This includes quasi-identifiers like date of birth, zip code, or occupation, which could potentially be used to re-identify individuals. Implement robust security measures to protect data from unauthorized access, breaches, loss, or damage. This includes physical security, encryption, access controls, and regular security audits. Ensure to store data in secure locations, such as password-protected computers, encrypted hard drives, or secure cloud storage with access controls. Encrypt data both in transit and at rest. This protects data from unauthorized access even if storage devices are lost or stolen. Restrict access to data to authorized personnel only. Use strong passwords and two-factor authentication, for this will maintain the integrity of data by preventing unauthorized modifications or corruption. Regularly back up data and store backups in a separate secure location. Ensure that backups are also encrypted. It is important to establish clear policies for how long data will be stored and when it will be securely deleted or disposed of and avoid keeping data longer than necessary.

Studying Health-Seeking Behaviour

A team of social scientists concerned with improvement of women's health wants to learn why women do not return to the hospital for the results of Papanicolaou (Pap) tests.¹ They have a research project to follow up with women who have a presumptive diagnosis of cervical cancer (a positive Pap test) but who do not return to the hospital, as advised, to receive their test results. The aim of the research is to find out how to improve services to these women. The chiefs of service in the hospital grant permission to the social scientists to conduct their investigations. Physicians provide the researchers with access to hospital records from which the researchers obtain the names and addresses of the patients. They then visit the patients in their homes. The social scientists identify themselves as researchers and ask permission to interview the patients in their homes. They then interview those patients who consent and give them information about the results of their Pap test.

The researchers inform the women that they should return to the hospital for follow-up care. They facilitate this process by giving the women the names of physicians that they can go to directly, thereby enabling them to avoid the usual bureaucratic obstacles. They defend their methodology by stating (1) that the study offers women health benefits; (2) that the study facilitates more rapid and easy access for women to the appropriate health services; and (3) that patients' records in public hospitals belong to the hospital and not to patients. Furthermore, the study is likely to reveal information that will enable the hospital to improve its services to women by effecting better follow-up, thereby reducing the rate of cervical cancer.

Source: WHO Casebook on Ethical Issues in International Research

Discussion Questions

1. Is it justified for the chiefs of service to grant permission to the social scientists to use the records without the consent of the patients? Is confidentiality breached?
2. Is it appropriate that the investigators visit the patients at their residence without permission?
3. Should social scientists provide the results of the Pap test to the patients?
4. In what other way could the investigators have approached the problem?

Data Use: Use data only for the purposes that were disclosed to individuals when it was collected. Avoid using data for new purposes without obtaining further consent. Ensure that data analysis and use do not lead to unfair discrimination against individuals or groups based on sensitive attributes like race, gender, or religion. Strive to use data in ways that benefit individuals and society while minimizing potential harm. Consider the potential consequences of data use and take steps to mitigate risks. Make sure to clarify who owns the data and who has the right to control its use. When transferring data across borders, ensure compliance with relevant data protection laws and regulations in all jurisdictions involved.

Take extra care when collecting and using data from vulnerable populations, such as children, the elderly, or people with disabilities.

5.4 Use of Placebo

Placebos are primarily used in clinical research, specifically in clinical trials designed to test the effectiveness of new treatments or interventions. However, placebo use in clinical trials is debated. Ethics and international guidance allow it in four situations: (1) no proven treatment exists; (2) withholding treatment poses negligible risk or is not life-threatening; (3) strong methodological reasons exist and withholding treatment poses no serious harm; and (4) (more controversially) strong methodological reasons the research aims to develop interventions for the participant population, and participants don't forgo needed treatment.

Conversely, placebos are inadmissible when effective treatments are available for a condition; in cases when the condition is life-threatening or can cause irreversible damage, when the risks of the placebo are significant, when the research design can be modified to avoid the use of a placebo control, and possibly when there is genuine uncertainty about the relative merits of the treatments being compared.

Individuals who agree to participate in the research must be fully informed about the possibility of receiving a placebo and must give their consent to participate in the research. Participants must be selected fairly and without bias. Deception should be avoided whenever possible. If deception is necessary, it must be justified by the research design and must be followed by a debriefing session in which participants are informed of the deception and the reasons for it. The potential benefits of the research must outweigh the risks of using a placebo. However, the researchers must take steps to minimize the risks of using a placebo, by carefully screening participants to exclude those who may be harmed by a placebo, by monitoring participants closely for adverse events, and providing participants with access to medical care if needed.

It is important to ensure that special care must be taken when using placebos with vulnerable populations, such as children, the elderly, or people with cognitive impairments.

5.4.1 Ethical considerations for use of placebos in Research

Although there are points of divergence among the documents, there is uniformity on the use of placebos, i.e. that if a proven effective intervention exists, the trial

intervention should generally be tested against it. Failure to do so deprives participants in the “control” arm of an intervention that is likely to benefit them. There are, however, some justifiable exceptions to this practice. For example, if a proven effective treatment exists, use of placebos may be acceptable if foregoing or delaying effective treatment poses only negligible or no serious risks to study participants.

- Guidelines from CIOMS, UNAIDS and WMA stipulate that there must be compelling methodological reasons for the use of placebos, e.g. if using the effective treatment as a comparator would not yield scientifically valid results.
- CIOMS, ICH and UNAIDS guidelines also stipulate that researchers must take steps to minimize any risks associated with the use of placebos.
- The Nuffield Council on Bioethics guidelines state that the use of placebos may be acceptable in LMICs if participants are not deprived of a treatment, they would have otherwise received but are provided at minimum with the standard of care that is the best available in the country’s public health system.

5.4.2 Use of placebos in Vaccine research

Few guidelines specifically address issues related to the use of placebos in vaccine trials, the UNAIDS guidelines being one notable exception.

The field of vaccine research is advancing rapidly. New technologies for developing vaccines may be foreign even to the general medical community. It is necessary to explain how and why a new vaccine is likely to protect against disease in ways easily understood by all stakeholders to allow better understanding of the issues associated with proposed trials.

Consideration about the types of potential placebos should be included in the broader discussion on trial design. A true placebo is an inert substance, but in the context of vaccine research, the term placebo is also applied to other types of comparators that are not inert but are not expected to protect against the disease of interest in a vaccine trial.

Vaccine trials in LMICs may be conducted in the following contexts: 1. A vaccine of proven efficacy in HICs is trialed in an LMIC (where it has not already been tested). Examples of these situations include the trials for vaccines against pneumococcal disease, rotavirus and human papillomavirus. 2. A new vaccine is trialed in an LMIC for

use against diseases that are largely confined to LMICs. Examples of these are trials for vaccines against conditions such as leishmaniasis, dengue fever and malaria.

When the efficacy of a vaccine is established in HICs, its efficacy in LMICs may remain uncertain and further placebo-controlled trials in LMICs may be necessary.

There are examples of a public health system not introducing a vaccine found to be beneficial to a specific population after a trial in that country. This has sometimes been due to the failure of the clinical trial sponsors to have prior discussions with policymakers and health authorities to clarify conditions necessary for the uptake of a new vaccine into the health system.

5.4.3 Acceptability of Use of Placebos

The use of placebos is clearly acceptable when no effective vaccine exists and the vaccine under consideration is intended to benefit the population in which the vaccine is to be tested.

The use of placebos is clearly unacceptable when an effective (or partially effective) and safe vaccine exists and is currently accessible in the public health system of the country in which the trial is planned and the risk to participants of not receiving the current vaccine cannot be mitigated adequately. Between these two extremes, several examples of ethical ambiguity exist. The use of placebos may sometimes be justified even if a vaccine of proven efficacy exists and the risks of using the placebo and withholding or delaying administration of the existing vaccine are greater than minimal.

Situations where Placebos may be Acceptable: Placebo-controlled trials may be justified in comparison to alternative study designs, even when an efficacious drug exists, provided that (a) the risks of using placebos are mitigated and justified by the scientific and social value of the research, (b) the research is responsive to local health needs, and (c) the general research ethics principles are respected.

1. A new (low-cost) investigational drug is being tested against a placebo, because while an effective drug exists, it is inaccessible to most of the population and is likely to remain so in the future. Accessibility may be hindered by limitations in a health system's ability to provide adequate support in areas such as administration, financing, production, distribution and infrastructure. Testing the new drug against the existing drug might not provide the desired information, i.e. how effective is the new drug compared to no drug (if having no drug is likely

to continue as the local standard of care)? When an existing drug is not in use in the trial country because of presumed barriers to access, researchers and sponsors proposing a placebo-controlled design should be prepared to provide evidence to local RECs and other stakeholders that these barriers are unlikely to be overcome in the foreseeable future. Although availability can change quickly when a new product reaches the market, researchers and sponsors should provide evidence that the new trial drug will not present the same barriers that have prevented the use of the existing drug

2. An existing drug is being tested against a placebo to confirm its efficacy in the trial country prior to uptake and introduction into the health system. As there is sometimes insufficient information and lack of consensus about the safety and efficacy of existing drug in different settings, the status of the existing drug as an “established effective treatment” in the local context may need to be determined.
3. A new drug is being tested against a placebo because scientific experts and health officials in the host country have determined that the existing drug(s) cannot be considered as an “established effective treatment” due to local epidemiological/demographic/environmental conditions, rendering it scientifically inappropriate as a comparator in a trial for the new drug. If reliable data on the safety and efficacy of the existing drug(s) in the local population are unavailable or unclear, using it as a comparator against a new drug in a trial would not provide sufficient information on the new drugs efficacy or effectiveness. In such situations, however, sponsors should first consult relevant experts regarding the legitimate reasons to doubt the efficacy or effectiveness of an existing drug in the trial population. Once it is established that there are good reasons to doubt the safety and/or efficacy of the existing drug in the trial population, the new drug may then be tested ethically against a placebo, provided the other conditions described above are met. When there is no reason to doubt the safety or effectiveness of an existing drug, testing the new drug against both a placebo and the existing drug would also provide evidence on the safety and effectiveness of the existing drug, while adequately answering the study question.
4. The existing licensed drug or a new developmental drug is being tested against a placebo because the public health significance of the drug’s introduction (i.e. its effect on the burden of morbidity and mortality due to the target disease) in the trial country is unknown or uncertain. Comparison with a placebo will yield clearer information on whether the introduction of the drug would have a public health impact.

5. A new drug is being tested against a placebo because the existing drug is unacceptable to the potential study participants in the trial country (for example, some populations object to drugs containing porcine gelatine, others reject vaccination administered by injection but will accept nasal sprays).

Testing a New HBV Vaccine

Of the five hepatitis viruses, hepatitis B (HBV) is the most serious since it can cause lifelong infections that place victims at high risk of death from cirrhosis of the liver and liver cancer – diseases that kill about a million people every year. Chronic HBV infections are most common in developing countries where most people who have the virus are infected during childhood through perinatal mother-to-child transmission or child-to-child transmission. Vaccines have been exceptionally effective for preventing chronic infections from developing but the cost has deterred their general distribution to children in high incidence, low-income countries. Two general types of hepatitis B vaccine have been widely used: plasma-derived vaccine and recombinant vaccine. The source of immunogens (HBsAg) used in these vaccines is different. The plasma-derived vaccine obtains HBsAg from the serum of persons chronically infected with HBV. The recombinant vaccine is produced using recombinant DNA technology and the HBsAg obtained is highly purified and inactivated.

Plasma-derived hepatitis B vaccine has been shown to be highly immunogenic and effective for prevention of acute and chronic HBV infection in infants, children, and adults. However, since the first reported case of HIV infection in 1981, safety concerns about plasma-derived vaccines have increased. New-generation recombinant vaccines have, however, proven as effective as plasma-derived vaccines in preventing HBV infection while avoiding potential transmission of HIV and other unknown agents associated with plasma-derived vaccines. A North American company has developed a novel hepatitis B recombinant vaccine. Phase I and II trials have demonstrated that the vaccine is safe, and preliminary results of a Phase III clinical trial have indicated good immune efficacy and safety in children and adults. Asia is a hyperendemic area for HBV infection, and the government of a large Asian country has approved an application to conduct a clinical trial of the vaccine in its jurisdiction. An institute in one of its largest cities has been provided with the resources to carry out a randomized, double-blind study with one experimental group and two control groups. The experimental group would receive the recombinant HBV vaccine, one control group would receive the plasma-derived HBV vaccine, and the second control group would receive a placebo.

Four hospitals in the city enrolled 240 infants born to HBsAg positive mothers, and therefore at high risk of becoming infected. The researchers briefed the infants' parents about the study, and explained the purpose and procedure of the research. For each child, at least one parent had to provide permission before their child could enrol in the study. The infants received the vaccine at birth, and then at 1 and 6 months of age. At 7 months after birth, a follow-up of each subject to evaluate the safety and protective efficacy of the vaccines took place. At the time the study was carried out, immunization with HBV vaccine was a paid service and was not covered by the national Expanded Programme on Immunization. The coverage rate of HBV vaccination was less than 20% in the city, which was located in the most highly developed area of the country.

Source: WHO Casebook on Ethical Issues in International Health Research

Questions for discussion

1. Is it ethical to set up the placebo control since 80% of the local children would not otherwise have received an HBV vaccine outside of this trial?
2. If you do not think the study meets current ethical standards, how could it be improved to conform to these standards?
3. Is it sufficient for investigators to seek permission from one parent of each child or should both parents must agree before a child could be entered in the vaccine trial?

5.5 Modifications and Waivers of Informed Consent

Informed consent is a cornerstone of ethical research. However, there are limited circumstances where it may be modified or waived. These waivers are granted only with strong justification and approval from the REC. Meaning all requests for waivers must be reviewed and approved by an REC. Waivers are not granted for convenience; researchers cannot seek a waiver simply to make the research easier or cheaper to conduct.

Waivers are acceptable in the following conditions: Research involving public benefit or service programs, Studies evaluating the effectiveness of public programs may involve a waiver if consent would make the research impractical, Research on educational practices, Studies conducted in educational settings may qualify for a waiver if the research examines common educational practices, and Research using existing data: Studies using existing data, documents, records, or specimens may be eligible for a waiver if the data is recorded in such a way that participants cannot be identified.

5.6 Other special considerations

Other special considerations in transnational research include:

- A. *Research Integrity*: There is an increase in research integrity concerns such as fraudulent data collection methods, low reproducibility of research findings, and falsification of study results. This impacts the reliability of research results. The Use of rigorous research methods, transparent reporting, and changing the research culture are critical to improve research integrity among scientists. Institutional support through clear guidelines, robust training, and mentorship is crucial to fostering a culture of research integrity

- B. *Conflict of Interest* arises when the potential for an individual or group gain compromises the professional judgment of policy makers or health-care providers. These are usually subtle, but they compromise decision making by policy makers and have potential to negatively impact public health. Conflict of interest occurs when policy makers are also involved in research, or if there are hidden financial relationships between the drug manufacturer and the researchers. Conflict of interest may also occur if policy decisions are made based on political influences as opposed to research evidence.

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6 Module 6: Continuing Education for REC Members

SCOPE OF THE MODULE

This module explores strategic approaches for enhancing the effectiveness and responsiveness of Research Ethics Committees (RECs) through continuous professional development, sharing of best practices, and inter-REC networking. As research methodologies and regulatory frameworks rapidly evolve, the ethical review process must adapt accordingly to uphold high standards of research integrity and participant protection.

LEARNING OBJECTIVES

By the end of this module, participants should be able to:

- Explain the importance of continuous education for Research Ethics Committee (REC) members
- Identify key evolving ethical issues and regulatory changes impacting research ethics
- Describe effective methods and tools for staying updated on ethical and regulatory developments
- Assess the value of sharing best practices and experiences among REC members
- Evaluate the benefits and challenges of networking among RECs
- Apply recommendations to enhance REC capacity through education, collaboration, and communication
- Analyze real-world cases to illustrate how RECs can respond to emerging challenges

6.1 Staying updated on evolving ethical issues and regulations

6.1.1 Highlighting the importance of ongoing education for REC members to keep abreast of new ethical challenges, advancements in research, and changes in regulatory landscapes

As the research landscape evolves due to technological advancements, globalization, and societal changes, REC members must engage in continuous education to effectively navigate new ethical challenges and regulatory updates.

The objective of staying updated on evolving ethical issues and regulations is to ensure that REC members are well-equipped to assess research proposals in line with the latest ethical standards, emerging challenges, and regulatory requirements.

6.1.2 Evolving Ethical Issues in Research

Advancements in research methodologies, such as the rise of artificial intelligence (AI) and machine learning, have introduced complex ethical concerns, for instance regarding confidentiality. Studies highlight issues related to privacy, algorithmic bias, and the use of big data, which require specialized knowledge for ethical oversight. Similarly, innovations in biotechnology, such as CRISPR-Cas9 for gene editing, have raised questions about the boundaries of permissible research and the potential for unintended societal consequences. REC members must remain informed about these developments to evaluate their ethical implications effectively.

6.1.3 Changes in Regulatory Landscapes

Regulatory frameworks governing research ethics are dynamic, reflecting shifts in societal values, scientific practices, and international norms. For instance, the Republic of Uganda Data Protection and Privacy Act, 2019 redefines consent to collect or process personal data. Additionally, global guidelines such as the Declaration of Helsinki and the Belmont Report are periodically updated to address emerging issues. Continuous education enables REC members to interpret and apply these regulations appropriately.

6.1.4 The Role of Ongoing Education

Ongoing education equips REC members with the skills and knowledge to address new ethical challenges and regulatory updates. It fosters critical thinking and ethical reasoning, which are essential for evaluating complex research proposals. Workshops, seminars, and online training programs tailored to specific ethical and regulatory topics have proven effective in enhancing the competencies of REC members (Guillemin et al., 2016).

6.1.5 Modes of staying updated on evolving ethical and regulatory issues

1. Formal training by attending courses and certified programs tailored to ethical and regulatory topics.
2. Regular briefings through REC meetings, newsletters, and ethics bulletins
3. Collaborations with experts in other fields like law, Information Technology, medicine, and other experts as a way of understanding complex issues as they arise.
4. Self-directed learning by members as a way of proactively gathering knowledge on relevant topics.

The above should focus on relevance and members' expertise and can be done as a;

1. Continuous process for example annual trainings in recurrent topics
2. Responsive updates to address urgent issues at hand
3. Pre-review preparations to ensure all members are aware of ethical issues for the protocols at hand.

6.1.6 Recommendations for Effective Training

Interdisciplinary Training: Incorporating diverse perspectives from law, bioethics, sociology, and technology ensures a comprehensive understanding of emerging issues.

Scenario-Based Learning: Simulations, learning by doing, and case studies of real-world ethical dilemmas enhance decision-making skills.

Regular Updates: Periodic training sessions aligned with updates in regulations and guidelines ensure REC members remain updated.

Global Collaboration: Engaging with international ethical bodies promotes knowledge exchange and harmonization of practices.

Data ethics: Updates on issues regarding data ownership, consent for storage or future use as secondary data, and compliance with changes in privacy regulations.

New Medical Procedure Study

A multicenter randomized controlled study of ablation procedure in the management of symptomatic Brugada syndrome. The REC was presented with a proposal to study the use of innovative radiofrequency ablation (RFA) procedure to prevent life-threatening abnormal heart rhythms in patients with Brugada syndrome. Brugada syndrome is a genetic condition that results in abnormal electrical activities within the heart. This condition leads to an increased risk of serious abnormal heart rhythms and subsequent sudden unexpected death. The current standard of care for patients with Brugada syndrome with life-threatening abnormal heart rhythms or sudden heart arrests (symptomatic Brugada syndrome) is the use of implantable cardiac defibrillator (ICD). The ICD is an implanted device that can detect abnormal heart rhythms and releases an electric shock to correct any life-threatening abnormal heart rhythms. However, several complications related to the ICD have been reported. These include inappropriate shock, device-related infections, and abnormal heart rhythm triggering and patients' anxiety and depression during the unexpected shock from the device.

Discussion Questions:

- a. What are the potential risks and benefits of this study?
- b. Share the observations and deficiencies flagged as inadequate in the consenting process which are to be addressed by the applicant.
- c. What concern(s) should be raised with regard to the potential risks of the new RFA approach?
- d. What measure(s) can be used to provide adequate participant protection?
- e. What strategies will be implemented to ensure that members of the REC are comprehensively knowledgeable on the new medical procedure?

6.2 Sharing best practices and experiences

6.2.1 Encouraging REC members to participate in conferences, workshops, and networking events to share experiences, learn from other RECs, and contribute to the development of best practices in research ethics review

The complex and dynamic nature of research ethics requires REC members to continually refine their approaches by learning from others. Sharing best practices and experiences through conferences, workshops, and networking events fosters collaboration, enhances decision-making, and ensures harmonization of ethical standards across institutions and regions.

The objective of sharing best practices and experiences is to strengthen the capacity of RECs by fostering a culture of continuous learning, collaboration, and standardization in ethical review processes.

6.2.2 Importance of Sharing Best Practices

REC members face diverse ethical challenges due to differences in research contexts, disciplines, and regulatory frameworks. Sharing experiences provides a platform to discuss these challenges and identify effective strategies. According to Guillemain et al. (2016), peer-to-peer learning among REC members improves their ability to handle complex ethical dilemmas, particularly in areas like informed consent, privacy protection, and conflict of interest. This collaborative approach also ensures that ethical reviews are not conducted in isolation but benefit from collective wisdom.

6.2.3 Conferences and Workshops as Learning Platforms

Conferences and workshops provide opportunities for REC members to engage with experts, exchange ideas, and stay updated on the latest developments in research ethics. Regional workshops tailored to specific ethical challenges, such as those organized by the World Health Organization (WHO), promote context-specific learning and capacity building.

6.2.4 Networking for Knowledge Exchange

Networking events enable REC members to establish connections with peers from different institutions and countries. These interactions facilitate the sharing of innovative practices, such as streamlined review processes and effective communication strategies with researchers. Research by Hyder et al. (2013) highlights that international collaborations among RECs can lead to the adoption of globally recognized ethical standards, ensuring consistency in research ethics review processes.

6.2.5 Contribution to the Development of Best Practices

By participating in collaborative forums, REC members contribute to the evolution of best practices in research ethics. For example, discussions during networking events often lead to the development of guidelines and policies that address emerging ethical challenges, such as those posed by digital health research and biobanking. These contributions not only benefit individual RECs but also strengthen the global research ethics community.

6.2.6 Recommendations for Effective Participation

Encourage Active Engagement: REC members should be encouraged to actively participate in discussions and share their unique experiences.

Promote Regional Collaboration: Regional networks of RECs can address context-specific ethical challenges and foster mutual support.

Leverage Technology: Virtual platforms can complement in-person events, making it easier for REC members to connect and share knowledge.

Document and Disseminate Best Practices: Summarizing key insights from conferences and workshops into accessible resources ensures that the knowledge is widely shared.

Research Involving a Product to Be Used Off-label

The efficacy and safety of X injection under laryngeal electromyography-guided in patients with unilateral vocal fold paralysis.

The ethics committee was presented with a proposed innovative off-label use of a product for addressing unilateral vocal cord paralysis (UVFP). UVFP is a clinical condition that at times presents following certain events, e.g., nerve injury during thyroidectomy or after stroke. When a patient suffers UVFP, the patient is susceptible to choking during swallowing, or hoarseness during phonating. The patient's quality of life is seriously affected and the patient is at risk for aspiration pneumonia. Such complications could be mild or severe, temporary or permanent. Normally the contralateral vocal cord increases in size and moves closer to the paralyzed cord to close the gap. In general practice patients are usually advised to wait for 6 months before opting for a surgical intervention. Such interventional approaches include medialization thyroplasty, arytenoid adduction, and laryngeal reinnervation. Usually these types of surgical correction are performed under general anesthesia. Prior the UVFP patients often examined with the assistance of videostroboscopy and/or laryngeal electromyography

Discussion Questions:

1. Should the proposed intervention be treated as a medical device or as a drug?
2. Does the proposed research present well defined risks that are significant and significantly understood? And is there available compensation for research-related
3. injury?
4. Is an "exemption from ethical review" appropriate in this case?

6.3 Networking with other RECs

6.3.1 Promoting collaboration and communication among RECs to foster consistency in ethical standards, share resources, and address common challenges.

Networking among RECs is increasingly recognized as an essential strategy for promoting consistency in ethical standards, sharing resources, and addressing common challenges.

By fostering collaboration and communication, networking enables RECs to strengthen their capacity to address the ethical complexities of modern research. This review examines the benefits, challenges, and strategies for effective networking among RECs.

6.3.2 Importance of Networking Among RECs

Networking allows RECs to align their practices with global ethical standards while considering local contexts. According to Hyder et al. (2013), collaboration among RECs leads to the harmonization of review processes, sharing of best practices, and is also relevant in overlapping ethics and integrity issues, such as conflicts of interest.

6.3.3 Promoting Consistency in Ethical Standards

Consistency in ethical standards is vital for ensuring fairness and credibility in research ethics review. Networking enables RECs to adopt unified guidelines, such as those provided by the Declaration of Helsinki or the Council for International Organizations of Medical Sciences (CIOMS). Collaborative efforts, such as the Pan-African Clinical Trials Registry, demonstrate how regional networks can establish standardized protocols for research ethics review.

6.3.4 Sharing Resources and Expertise

Resource constraints, particularly in low- and middle-income countries, can hinder the effectiveness of RECs. Networking provides a platform for resource sharing, such as access to training materials, policy templates, and expert consultations. For instance, the Forum for Ethical Review Committees in the Asian and Western Pacific Region (FERCAP) has successfully facilitated capacity building through its regional networks.

6.3.5 Addressing Common Challenges

Networking helps RECs collectively address shared challenges, such as managing conflicts of interest, ensuring data privacy, and navigating cultural differences in ethical decision-making. Collaborative forums enable REC members to discuss and develop strategies for emerging ethical dilemmas, such as those posed by artificial intelligence and biobanking.

6.3.6 Challenges in Networking

Despite its benefits, networking among RECs faces challenges such as logistical barriers, resource limitations, and differences in regulatory frameworks. Studies suggest that the lack of sustained funding and coordination can hinder the effectiveness of REC networks. Addressing these challenges requires strategic planning and institutional support.

6.3.7 Recommendations for Effective Networking

1. Establish Regional and International Networks: Formal networks, such as the African Research Ethics Network (AREN), provide platforms for collaboration and knowledge exchange.
2. Leverage Technology: Online platforms and virtual meetings can facilitate communication among geographically dispersed RECs.
3. Encourage Policy Harmonization: Developing region-specific guidelines aligned with international standards ensures consistency in ethical review.
4. Provide Training and Capacity Building: Joint training programs enhance the competencies of REC members and foster mutual understanding.

An application submitted to several African countries involving a new vaccine during an outbreak.

Differences in ethical review processes across countries can delay trial approvals, affecting the timely rollout of the trial. A regional ethics task force can be created to align review processes. Joint reviews can be established, and Partner countries can agree to accept approvals from the joint ethics review.

Discussion Questions:

- a. Outline the differences in ethical review processes across countries that can delay trial approvals, affecting the timely rollout of the trial.
- b. What measures can be taken to improve the timelines of review and approval?

6.4 Learning and Teaching Methodologies

This course module uses interactive lectures and scenario-based learning.

For interactive lectures, multiple speakers present on each issue, providing diverse perspectives. For instance, an academic ethicist could discuss ethical principles, a researcher could discuss medical information, and a community representative could discuss cultural issues related to transnational research including Adaptive Trial designs. Additionally, interactive lectures allow for immediate feedback and clarification on any areas of confusion, ensuring that members are well-equipped to navigate the ethical challenges they may encounter in their roles.

For scenario-based learning, it will involve presenting learners with a realistic situation or ethical dilemma, and encourage them to analyze the issue, make decisions, and reflect on their reasoning. This will bridge theory and practice.

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